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L4	antazoline	481	L4
L3	L2 and ophthalmic	38	L3
L2	L1 and pheniramine	98	L2
L1	ketotifen	960	L1

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                   with the 228th ACS National Meeting
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=> s ophthalmic (5a) (ketotifen or pheniramine)
L1          175 OPHTHALMIC (5A) (KETOTIFEN OR PHENIRAMINE)

=> dup remove L1
PROCESSING COMPLETED FOR L1
L2           90 DUP REMOVE L1 (85 DUPLICATES REMOVED)

=> d l2 1-90 bib, ab

L2   ANSWER 1 OF 90  CA  COPYRIGHT 2004 ACS on STN     DUPLICATE 1
AN   141:59723  CA
TI   Storage-stable compositions containing ketotifen and imidazolines, and
     method for improvement of light stability of ketotifen with amino acids
IN   Inoue, Makoto; Nitta, Hiroo
PA   Rohto Pharmaceutical Co., Ltd., Japan
SO   Jpn. Kokai Tokkyo Koho, 27 pp.
     CODEN: JKXXAF
DT   Patent
LA   Japanese
FAN.CNT 1
     PATENT NO.          KIND   DATE        APPLICATION NO.         DATE
     ---------------     ----   --------    --------------------    --------
PI   JP 2004175770        A2    20040624    JP 2002-347312          20021129
PRAI JP 2002-347312             20021129
OS   MARPAT 141:59723
AB   The compns. contain ketotifen or its salts, imidazolines I [Z indicates
     hydrocarbon ring or heterocycle; R1 = R1a, (R1b)sNR2b, R1cO; R1a, R1b, R1c
     = alkylene; R2b = H, alkyl; s = 0, 1; R2 = substituent; m = 0, 1; n 0-6]
     or their salts, and amino acids H2N(CH2)tCO2H (t = 1-5).  An aqueous solution
     containing 69 mg ketotifen fumarate, 3 mg naphazoline-HCl, and 5.0 g
     e-aminocaproic acid showed absorbance at 400 nm of 0.019 after exposure to
     light of 200,000 lx-h.  Photodecompn. of ketotifen was prevented.
     Formulation examples of eye drops and nasal drops are given.

L2   ANSWER 2 OF 90  CA  COPYRIGHT 2004 ACS on STN     DUPLICATE 2
AN   140:412326  CA
```

TI **Ophthalmic** solutions containing **ketotifen** fumarate, menthol, and chlorobutanol
IN Usui, Takeshi; Egami, Fumiyasu
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2004143158	A2	20040520	JP 2003-336738	20030929
PRAI JP 2002-288417	A	20021001		

AB The ophthalmic solns. cause no ocular pain and show long-lasting antipruritic effect. Thus, a composition containing ketotifen fumarate 13.8, tetrahydrozoline hydrochloride 50, di-K glycyrrhizate 250, chlorpheniramine maleate 30, aminoethylsulfonic acid 1000, vitamin B6 100, vitamin E 50, menthol 10, chlorobutanol 100, glycerin 1650, polysorbate 80 100, benzalkonium chloride 10, mg, NaOH, and H2O to 100 mL was applied to eyes of healthy volunteers to cause pain.

L2 ANSWER 3 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 3
AN 140:412325 CA
TI Nonirritant **ophthalmic** solutions containing **ketotifen** fumarate and polymers
IN Sugita, Kimiko; Egami, Fuminobu
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2004143157	A2	20040520	JP 2003-336262	20030926
PRAI JP 2002-288434	A	20021001		

AB Ophthalmic solns., which cause no ocular pain, contain (a) ketotifen fumarate (I) and (b) ≥1 polymer selected from hydroxypropyl Me cellulose (II), hydroxyethyl cellulose, carboxyvinyl polymers, and poly(vinyl alc.). Thus, a composition containing I 69, II 100, glycerin 2500 mg, NaOH, and H2O to 100 mL was applied to eyes of healthy volunteers to slightly cause ocular pain.

L2 ANSWER 4 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 4
AN 140:412324 CA
TI **Ophthalmic** solutions containing **ketotifen** fumarate, vasoconstrictors, and chlorobutanol
IN Usui, Takeshi; Egami, Fuminobu
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2004143156	A2	20040520	JP 2003-336258	20030926
PRAI JP 2002-288427	A	20021001		

AB The ophthalmic solns. cause no ocular pain and show long-lasting antipruritic effect. Thus, a composition containing ketotifen fumarate 13.8, tetrahydrozoline hydrochloride 50, chlorobutanol 100, glycerin 2475, polysorbate 80 100, benzalkonium chloride 10 mg, pH controller, and H2O to 100 mL was applied to eyes of healthy volunteers to cause slight ocular

pain and suppress ocular itching for 15-30 min.

L2 ANSWER 5 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 5
AN 140:412323 CA
TI **Ophthalmic** solutions containing **ketotifen** fumarate and sodium chondroitin sulfate and/or sodium hyaluronate
IN Ouchi, Junko; Egami, Fuminobu
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2004143155	A2	20040520	JP 2003-336255	20030926
PRAI JP 2002-288424	A	20021001		

AB The ophthalmic solns. cause no ocular pain and suppress ocular itching in pollenosis, etc. The solns. may be also used as collyriums. Thus, an **ophthalmic** solution was prepared from **ketotifen** fumarate 69, Na chondroitin sulfate 500, chlorobutanol 150, glycerin 2500, polysorbate 80 100, benzalkonium chloride 5 mg, NaOH, and H2O to 100 mL. Application of the solution to eyes of volunteers caused no ocular pain and suppressed ocular discomfort for .apprx.10 min.

L2 ANSWER 6 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 6
AN 140:412337 CA
TI **Ophthalmic** solutions containing **ketotifen** fumarate, vasoconstrictors, and ε-aminocaproic acid
IN Ouchi, Junko; Saito, Naoko; Usui, Takeshi; Egami, Fuminobu; Sugita, Kimiko
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2004143154	A2	20040520	JP 2003-336240	20030926
PRAI JP 2002-288407	A	20021001		

AB The ophthalmic solns. show enhanced antiallergic and antiinflammatory effects, thus effectively suppress conjunctival hyperemia and edema. The ophthalmic solns. may addnl. contain ≥1 selected from H2NCH2CH2SO3H, aspartic acid salts, and glycyrrhizic acid salts. A composition containing ketotifen fumarate 69 mg, tetrahydrozoline hydrochloride 50 mg, ε-aminocaproic acid 5000 mg, and H2O to 100 mL effectively suppressed allergic symptoms in guinea pigs having Japanese cedar pollinosis.

L2 ANSWER 7 OF 90 USPATFULL on STN
AN 2004:83151 USPATFULL
TI Process to improve stability of a pharmaceutical composition
IN Fetz, Andrea, Wetzikon, SWITZERLAND
Kis, Georg Ludwig, Triboltingen, SWITZERLAND
Pepiot, Michel, Annonay, FRANCE
PI US 2004063607 A1 20040401
AI US 2003-451088 A1 20030617 (10)
WO 2001-EP15126 20011220
PRAI EP 2000-12838 20001222
DT Utility
FS APPLICATION
LREP THOMAS HOXIE, NOVARTIS, CORPORATE INTELLECTUAL PROPERTY, ONE HEALTH PLAZA 430/2, EAST HANOVER, NJ, 07936-1080
CLMN Number of Claims: 12

ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 360
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention describes in particular a method for stabilizing a pharmaceutical composition by contacting said composition with a polymeric material comprising in particular an ethylene oxide sterilization step.

L2 ANSWER 8 OF 90 USPATFULL on STN
AN 2004:205837 USPATFULL
TI Ophthalmic composition
IN Adam, Marcia Johanna, Gisikon, SWITZERLAND
Fetz, Andrea, Wetzikon, SWITZERLAND
Kis, Gyorgy Lajos, Triboltingen, SWITZERLAND
PA Novartis AG, Basel, SWITZERLAND (non-U.S. corporation)
PI US 6777429 B1 20040817
AI US 2000-619349 20000719 (9)
PRAI EP 1999-114508 19990723
DT Utility
FS GRANTED
EXNAM Primary Examiner: Fay, Zohreh
LREP Hess, Susan L., Wildman, David E.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 147
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is related to an **ophthalmic** composition comprising **ketotifen** as a pharmaceutically active agent.

L2 ANSWER 9 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2004:367127 BIOSIS
DN PREV200400371911
TI Autoclavable pharmaceutical compositions containing a chelating agent.
AU Kis, Gyorgy Lajos [Inventor, Reprint Author]; Adam, Marcia Johanna [Inventor]; Fetz, Andrea [Inventor]
CS Triboltingen, Switzerland
ASSIGNEE: Novartis AG, Basel, Switzerland
PI US 6776982 August 17, 2004
SO Official Gazette of the United States Patent and Trademark Office Patents, (Aug 17 2004) Vol. 1285, No. 3. http://www.uspto.gov/web/menu/patdata.html . e-file.
ISSN: 0098-1133 (ISSN print).
DT Patent
LA English
ED Entered STN: 8 Sep 2004
Last Updated on STN: 8 Sep 2004
AB Disclosed are **ophthalmic** compositions comprising **ketotifen** and pharmaceutically acceptable salts thereof, as well as methods for making such compositions.

L2 ANSWER 10 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2004:375024 BIOSIS
DN PREV200400381830
TI Ophthalmic composition.
AU Adam, Marcia Johanna [Inventor, Reprint Author]; Fetz, Andrea [Inventor]; Kis, Gyorgy Lajos [Inventor]
CS Gisikon, Switzerland
ASSIGNEE: Novartis AG, Basel, Switzerland
PI US 6774137 August 10, 2004
SO Official Gazette of the United States Patent and Trademark Office Patents,

(Aug 10 2004) Vol. 1285, No. 2. http://www.uspto.gov/web/menu/patdata.html . e-file.
ISSN: 0098-1133 (ISSN print).
DT Patent
LA English
ED Entered STN: 22 Sep 2004
Last Updated on STN: 22 Sep 2004
AB The present invention is related to an **ophthalmic** composition comprising **ketotifen** as a pharmaceutically active agent.

L2 ANSWER 11 OF 90 MEDLINE on STN
AN 2004418880 IN-PROCESS
DN PubMed ID: 15324519
TI Efficacy and comfort of olopatadine versus **ketotifen** **ophthalmic** solutions: a double-masked, environmental study of patient preference.
AU Leonardi Andrea; Zafirakis Panayotis
CS Ophthalmology Unit, University of Padova, Padova, Italy.. andrea.leonardi@unipd.it
SO Current medical research and opinion, (2004 Aug) 20 (8) 1167-73. Journal code: 0351014. ISSN: 0300-7995.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20040825
Last Updated on STN: 20040915
AB BACKGROUND: Ocular allergies cause itching, redness, chemosis, tearing, and swelling of the eyelids in sensitized individuals. The options available for treatment of ocular allergy include olopatadine 0.1% (Opatanol; Patanol [US]) and ketotifen 0.025% (Zaditen; Zaditor [US]). Patient preference for an eye drop can often be a primary factor in determining the level of compliance and satisfaction with any given therapy. OBJECTIVE: This study sought patient perspective on eye drop efficacy in controlling signs and symptoms of allergic conjunctivitis and eye drop comfort. Also evaluated were the factors considered by patients when making decisions of preference. METHODS: One hundred patients with previous history and current symptoms of seasonal or perennial allergic conjunctivitis were enrolled at two centers (Athens, Greece, N = 50; Padova, Italy, N = 50) for this two visit, double-masked study. Qualified patients received two masked bottles of medication (one olopatadine, one ketotifen) and were asked to use both medications as needed over the course of four weeks, but not to exceed usage of two drops of medication per eye per day. At the second visit, patients answered five questions comparing the two masked medications in terms of preference, drop comfort, and efficacy in treatment of signs and symptoms. Patients also defined the factors upon which they based these decisions. RESULTS: A significantly greater percentage of patients (81%) selected olopatadine when asked which medication they preferred; which they found more comfortable; which they found more efficacious in reducing symptoms of allergy; and which they would select if visiting the doctor's office ($P < 0.0001$). Seventy-six percent (76%) of patients considered both efficacy and comfort when making their preference decisions ($P < 0.0001$). No adverse events were volunteered or elicited. CONCLUSION: In this study, patients preferred to use the anti-allergy eye drop olopatadine over ketotifen after using both drops and evaluating relative efficacy and comfort during the course of four weeks. A significantly greater percentage of the patients preferred to use olopatadine during the study period, found it more efficacious and comfortable, and would select olopatadine if visiting their doctor's office during allergy season.

L2 ANSWER 12 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 7
AN 139:122746 CA
TI Safe ophthalmic compositions containing trometamol and no or reduced

amount of quaternary ammonium-based surfactants, and showing good antiseptic activity
IN Kobayashi, Minoru; Miyamoto, Hiromi; Watanabe, Shizuaki; Kimura, Takahito
PA Teika Seiyaku Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 16 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2003206241	A2	20030722	JP 2002-4250	20020111
JP 2004043516	A2	20040212	JP 2003-392022	20031121
PRAI JP 2002-4250	A3	20020111		

AB Title compns. contain low-mol. weight pharmacol. active substances and H2NC(CH2OH)3. Thus, a transparent ophthalmic solution containing pemirolast K salt 100, H2NC(CH2OH)3 300, and benzalkonium 0.5 mg showed good antibacterial activity.

L2 ANSWER 13 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 8
AN 138:95648 CA
TI Eyedrops containing ketotifen
IN Sawa, Shiro
PA Senju Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2003026565	A2	20030129	JP 2001-209065	20010710
PRAI JP 2001-209065		20010710		

AB This invention relates to eyedrops containing ketotifen or salts thereof and sorbic acid or its salts to facilitate the transfer of the ketotifen to conjunctiva. For example, an eyedrop solution contained ketotifen fumarate 0.069, NaCl 0.85, NaOAc 0.1, sorbic acid 0.3 g, NaOH/HCl q.s. to pH 5, and distilled water to 100 mL.

L2 ANSWER 14 OF 90 USPATFULL on STN
AN 2003:335420 USPATFULL
TI 1,3-bis-(substituted-phenyl)-2-propen-1-ones and their use to treat VCAM-1 mediated disorders
IN Meng, Charles Q., Alpharetta, GA, UNITED STATES
Ni, Liming, Duluth, GA, UNITED STATES
Sikorski, James A., Alpharetta, GA, UNITED STATES
Hoong, Lee K., Suwanee, GA, UNITED STATES
PA Atherogenics Pharmaceuticals, Inc. (U.S. corporation)
PI US 2003236298 A1 20031225
AI US 2003-443470 A1 20030521 (10)
RLI Continuation of Ser. No. US 2001-1868, filed on 19 Nov 2001, GRANTED, Pat. No. US 6545007
PRAI US 2000-249532P 20001117 (60)
DT Utility
FS APPLICATION
LREP KING & SPALDING, 191 PEACHTREE STREET, N.E., ATLANTA, GA, 30303-1763
CLMN Number of Claims: 84
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 4684
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB It has been discovered certain 1,3-bis-(substituted-phenyl)-2-propen-1-ones, including compounds of formula (I) inhibit the expression of VCAM-1, and thus can be used to treat a patient with a disorder mediated

by VCAM-1. Examples of inflammatory disorders that are mediated by VCAM-1 include, but are not limited to arthritis, asthma, dermatitis, cystic fibrosis, post transplantation late and chronic solid organ rejection, multiple sclerosis, systemic lupus erythematosis, inflammatory bowel diseases, autoimmune diabetes, diabetic retinopathy, rhinitis, ischemia-reperfusion injury, post-angioplasty restenosis, chronic obstructive pulmonary disease (COPD), glomerulonephritis, Graves disease, gastrointestinal allergies, conjunctivitis, atherosclerosis, coronary artery disease, angina and small artery disease.

L2 ANSWER 15 OF 90 USPATFULL on STN
AN 2003:44408 USPATFULL
TI Ophthalmic compositions and use
IN Wong, Michelle, Duluth, GA, UNITED STATES
Sou, Mary, Alpharetta, GA, UNITED STATES
Yen, Shau-fong, Atlanta, GA, UNITED STATES
Minick, Kasey, Cary, NC, UNITED STATES
PI US 2003031718 A1 20030213
AI US 2002-164756 A1 20020607 (10)
PRAI US 2001-297068P 20010608 (60)
DT Utility
FS APPLICATION
LREP THOMAS HOXIE, NOVARTIS CORPORATION, PATENT AND TRADEMARK DEPT, 564 MORRIS AVENUE, SUMMIT, NJ, 079011027
CLMN Number of Claims: 34
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 706
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are a once-a-day **ophthalmic** drug composition, comprising in particular **ketotifen**, comprising a polymer comprising chitosan and a carrier, and a method to treat an ocular allergy comprising administering a once-a-day **ophthalmic** **ketotifen** composition comprising chitosan to the eye of a mammal.

L2 ANSWER 16 OF 90 USPATFULL on STN
AN 2003:222128 USPATFULL
TI 1, 3-bis-(substituted-phenyl)-2-propen-1-ones and their use to treat VCAM-1 mediated disorders
IN Ni, Liming, Duluth, GA, United States
Hoong, Lee K., Suwanee, GA, United States
Sikorski, James A., Alpharetta, GA, United States
Meng, Charles Q., Alpharetta, GA, United States
PA Atherogenics, Inc., Alpharetta, GA, United States (U.S. corporation)
PI US 6608101 B1 20030819
AI US 2001-886348 20010620 (9)
PRAI US 2000-212769P 20000620 (60)
US 2000-255934P 20001215 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Lambkin, Deborah C.
LREP Knowles, Sherry M., King & Spalding, LLP.
CLMN Number of Claims: 49
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 4228
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB It has been discovered certain 1,3-bis-(substituted-phenyl)-2-propen-1-ones, including compounds of formula (I) inhibit the expression of VCAM-1, and thus can be used to treat a patient with a disorder mediated by VCAM-1. Examples of inflammatory disorders that are mediated by VCAM-1 include, but are not limited to arthritis, asthma, dermatitis, cystic fibrosis, post transplantation late and chronic solid organ

rejection, multiple sclerosis, systemic lupus erythematosis, inflammatory bowel diseases, autoimmune diabetes, diabetic retinopathy, rhinitis, ischemia-reperfusion injury, post-angioplasty restenosis, chronic obstructive pulmonary disease (COPD), glomerulonephritis, Graves disease, gastrointestinal allergies, conjunctivitis, atherosclerosis, coronary artery disease, angina and small artery disease.

L2 ANSWER 17 OF 90 USPATFULL on STN
AN 2003:155670 USPATFULL
TI Method for treating pharmaceutical compositions
IN Kis, Gyorgy Lajos, Triboltingen, SWITZERLAND
PA Novartis AG, Basel, SWITZERLAND (non-U.S. corporation)
PI US 6576649 B1 20030610
AI US 2000-627799 20000728 (9)
RLI Continuation of Ser. No. WO 1999-EP2221, filed on 31 Mar 1999, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Fay, Zohreh
LREP Wildman, David E.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 431
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention describes in particular a method for stabilizing a pharmaceutical composition by contacting said composition with a polymeric material comprising an antioxidant.

L2 ANSWER 18 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 9
AN 140:12689 CA
TI A placebo-controlled comparison of **ketotifen** fumarate and nedocromil sodium **ophthalmic** solutions for the prevention of ocular itching with the conjunctival allergen challenge model
AU Greiner, Jack V.; Minno, George
CS Schepens Eye Research Institute, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA
SO Clinical Therapeutics (2003), 25(7), 1988-2005
CODEN: CLTHDG; ISSN: 0149-2918
PB Excerpta Medica, Inc.
DT Journal
LA English
AB Background: **Ketotifen** fumarate 0.025% **ophthalmic** solution and nedocromil sodium 2.0% ophthalmic solution are 2 topical antiallergic medications with different modes of action and efficacy profiles. Both solns. are indicated for ocular itching associated with allergic conjunctivitis. Objective: This study compared the efficacy, safety, and comfort of **ketotifen** fumarate 0.025% **ophthalmic** solution and nedocromil sodium 2.0% ophthalmic solution for the prevention of ocular itching, using the conjunctival allergen challenge (CAC) model. Methods: This was a single-center, double-masked, contralateral, randomized, placebo- and active-controlled CAC clin. trial. Subjects aged >10 yr with a history of allergic hypersensitivity who responded to the CAC at screening visits 1 and 2 qualified for randomization at visit 3. At visit 3 (day 21) and visit 4 (day 35), subjects received 1 of 3 treatments: ketotifen, nedocromil, or placebo (artificial tears), randomized by eye. Allergen challenges were conducted at 5 min posttreatment dose (visit 3) and 12 h posttreatment dose (visit 4). At each visit, subjects evaluated their ocular itching every 30 s for 20 min. At visit 4, subjects evaluated the comfort of the medication immediately after instillation, at 30 s after instillation, and at 1, 2, 5, and 10 min after instillation. The subjects were also queried about overall eyedrop comfort by choosing from descriptive terms and about overall eyedrop preference based on comfort and perceived efficacy. Results: Eighty-five subjects were

screened for this study. Fifty-nine (28 males, 31 females; mean age, 38.7 yr) qualified and were randomized to receive study medications. Ketotifen-treated eyes experienced significantly less ocular itching induced by CAC than nedocromil-treated eyes and those that received placebo at both the 5-min and 12-h posttreatment allergen challenges (all $P < 0.05$). Nedocromil-treated eyes showed no statistical or clin. differences from placebo at any time point. Ketotifen-treated eyes showed no differences in comfort from those that received placebo but were significantly more comfortable than nedocromil-treated eyes at 1, 2, 5, and 10 min after instillation (all $P < 0.05$). On the basis of comfort and subjective efficacy, 60% of subjects preferred ketotifen, 21% preferred nedocromil, and 19% preferred placebo. Conclusion: Ketotifen was significantly more effective and comfortable than nedocromil at both 5 min and 12 h after administration in this CAC model.

RE.CNT 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 19 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 10
AN 140:12688 CA
TI Comparison of **ketotifen** fumarate **ophthalmic** solution alone, desloratadine alone, and their combination for inhibition of the signs and symptoms of seasonal allergic rhinoconjunctivitis in the conjunctival allergen challenge model: a double-masked, placebo- and active-controlled trial
AU Crampton, H. Jerome
CS Ophthalmic Research Associates, North Andover, MA, USA
SO Clinical Therapeutics (2003), 25(7), 1975-1987
CODEN: CLTHDG; ISSN: 0149-2918
PB Excerpta Medica, Inc.
DT Journal
LA English
AB Background: Ketotifen fumarate is a topical antiallergic combination mast-cell stabilizer and antihistamine indicated for the temporary prevention of ocular itching due to allergic conjunctivitis. Desloratadine is a systemic antihistamine indicated for the treatment of seasonal and perennial allergic rhinitis. Objective: The purpose of this study was to compare the efficacy of **ketotifen** 0.025% **ophthalmic** solution instilled in the eye, desloratadine 5-mg tablets taken orally, and their combination for prevention of the signs and symptoms of allergic rhinoconjunctivitis, as induced by the conjunctival allergen challenge (CAC) model. Methods: This was a randomized, double-masked, placebo- and active-controlled, single-center clin. trial. At visit 1, the dose of allergen necessary to elicit a qualifying allergic reaction was determined for subjects meeting the entry criteria. At visit 2, the allergen dose determined at visit 1 was confirmed, and all subjects who had a qualifying ocular and nasal allergic reaction were randomized to 1 of 3 treatment groups: **ketotifen ophthalmic** solution and placebo tablet, desloratadine tablet and placebo eyedrop, or ketotifen and desloratadine. Subjects were instructed to instill 1 drop into each eye twice daily and take 1 tablet with water once daily at the same time as the morning eyedrop for .apprx.4 wk. At visit 3, subjects brought in their medication and were given 1 drop of the eyedrop bilaterally and 1 tablet with water. Bilateral CAC was performed 2 h after administration of medication. Using standardized scales, subjects rated ocular itching at 3, 5, and 7 min after CAC; ocular tearing and eyelid swelling at 10, 15, and 20 min after CAC; and nasal signs and symptoms (sneezing, rhinorrhea and postnasal drip, pruritus, and nasal congestion) at 10, 20, 30, 40, and 50 min after CAC. The investigator graded ocular redness and chemosis at 10, 15, and 20 min after CAC. At all visits, subjects were offered an anti-allergy eyedrop to relieve any immediate ocular discomfort caused by CAC. Results: One hundred two subjects were screened-82 (55 women, 27 men; mean age, 42.8 yr [range, 21-70 yr]) were randomized to treatment, and 80 completed the study. Subjects in the group that received ketotifen (n = 27) and the group that received ketotifen with

desloratadine (n = 26) had significantly lower mean itching scores compared with those in the group that received desloratadine alone (n = 27) at all time points ($P \leq 0.05$). Total ocular redness, calculated by summing the mean redness scores for each of the 3 vessel beds, was significantly lower in the ketotifen group than in the other treatment groups at most time points ($P \leq 0.05$). All treatments attenuated nasal symptoms; no statistically significant differences were noted between treatment groups, with the exception of the 50-min time point, at which combination treatment was significantly more effective than ketotifen alone ($P \leq 0.05$). The proportion of subjects who requested relief drops after CAC was significantly lower in both the ketotifen alone and combination treatment groups compared with the desloratadine alone group ($P = 0.004$). Conclusions: **Ketotifen ophthalmic** solution significantly decreased the signs and symptoms of ocular and nasal allergic rhinoconjunctivitis. The addition of ketotifen to the oral desloratadine regimen improved the overall antiallergic efficacy of both medications.

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 20 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 11

AN 2003:573227 BIOSIS

DN PREV200300578182

TI Efficacy and safety of ketotifen eye drops in the treatment of seasonal allergic conjunctivitis.

AU Kidd, M. [Reprint Author]; McKenzie, S. H.; Steven, I.; Cooper, C.; Lanz, R.; Australian Ketotifen Study Group

CS Department of General Practice, University of Sydney, Sydney, NSW, Australia
michael.kidd@med.usyd.edu.au

SO British Journal of Ophthalmology, (October 2003) Vol. 87, No. 10, pp. 1206-1211. print.
ISSN: 0007-1161 (ISSN print).

DT Article

LA English

ED Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003

AB Background: Ketotifen blocks histamine H1 receptors, stabilises mast cells, and prevents eosinophil accumulation. These multiple, pharmacological mechanisms provided the rationale for assessing the efficacy and safety of ketotifen 0.025% eye drops in subjects with seasonal allergic conjunctivitis (SAC) in an environmental setting. Methods: This was a double masked, randomised, multicentre trial conducted in Australia. Subjects were randomly assigned to **ketotifen** fumarate 0.025% **ophthalmic** solution, placebo (as vehicle), or levocabastine hydrochloride 0.05% ophthalmic suspension, twice daily in each eye for a 4 week period. Subjects were assessed at follow up (days 5-8) and termination (days 25-31) visits. The primary efficacy variable was the responder rate, based on the subjects' assessment of global efficacy at the follow up visit. Results: 519 subjects were randomised to treatment. At the follow up visit, the responder rate, based on subjects' assessment of global efficacy, was significantly greater in the ketotifen group (49.5%) than in the placebo group (33.0%) for subjects with a positive diagnostic test for pollen allergy ($p=0.02$). The investigators' assessment of responder rates also showed that ketotifen was superior to placebo ($p=0.001$). Ketotifen produced a significantly better outcome than levocabastine ($p<0.05$) for relief of signs and symptoms of SAC, at both the follow up and the termination visit. The type and frequency of adverse events were similar across treatment groups. Conclusions: In an environmental setting, **ketotifen** fumarate 0.025% **ophthalmic** solution was well tolerated and effective in reducing the signs and symptoms of SAC, and in preventing their recurrence. Ketotifen consistently showed the best efficacy in comparison with both

placebo and levocabastine. These results indicate that ketotifen eye drops are a valuable treatment option for this condition.

L2 ANSWER 21 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 12
AN 141:17502 CA
TI Efficacy and safety of ketotifen fumarate 0.025% in the conjunctival antigen challenge model of ocular allergic conjunctivitis
AU Greiner, Jack V.; Mundorf, Thomas; Dubiner, Harvey; Lonsdale, John; Casey, Richard; Parver, Leonard; Kapik, Barry M.; Shams, Naveed B. K.; Abelson, Mark B.
CS Schepens Eye Research Institute, Harvard Medical School, Boston, MA, USA
SO American Journal of Ophthalmology (2003), 136(6), 1097-1105
CODEN: AJOPAA; ISSN: 0002-9394
PB Elsevier Science Inc.
DT Journal
LA English
AB Purpose: To determine the duration of action of ketotifen 0.025% eye drops vs placebo taken as single or multiple doses in an allergen challenge model. Design: Two randomized, multicenter, double-masked, contralateral placebo-controlled studies, one a single-dose and one a multiple-dose study. Methods: Two conjunctival provocation tests (CPTs) were initially conducted to confirm reproducibility of subject responses in both studies. Subjects in study 1 (n = 87) received single doses of ketotifen in one eye and placebo in the other 15 min, 6 h, and 8 h before CPT. Subjects in study 2 (n = 85) received ketotifen or placebo once 8 h before CPT. Single-dose efficacy results were used to further qualify a subject as a responder. Responders were re-randomized to a 4-wk twice daily dosing regimen with a CPT 8 h after the final dose. In both studies, ocular symptoms were assessed at three time points 3 to 15 min after challenge. There were no significant differences in adverse events between groups. Results: For both studies, ocular itching and vascular injection were significantly reduced (P <.003) at all time points after instillation of ketotifen, with a maximum reduction at 7 min postchallenge. In study 2, chemosis, tearing, and lid swelling were also assessed and were significantly reduced (P <.008) after instillation of ketotifen. Conclusions: Ketotifen 0.025% eye drops were safe and statistically effective in preventing ocular itching, injection, and other signs and symptoms of allergic conjunctivitis at 15 min, 6 h, and 8 h after a single dose and at 8 h after the final dose of a 4-wk twice daily regimen.
RE.CNT 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 22 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 13
AN 139:111402 CA
TI Efficacy of **ketotifen** fumarate 0.025% **ophthalmic** solution compared with placebo in the conjunctival allergen challenge model
AU Abelson, Mark B.; Chapin, Matthew J.; Kapik, Barry M.; Shams, Naveed B. K.
CS Schepens Eye Research Institute and Department of Ophthalmology, Harvard Medical School, Boston, USA
SO Archives of Ophthalmology (Chicago, IL, United States) (2003), 121(5), 626-630
CODEN: AROPAW; ISSN: 0003-9950
PB American Medical Association
DT Journal
LA English
AB Background: Ketotifen fumarate blocks histamine1 (H1) receptors, stabilizes mast cells, and acts as an eosinophil inhibitor (decreases chemotaxis and activation of eosinophils). Objective: To assess the efficacy of **ketotifen** 0.025% **ophthalmic** solution in the prevention of symptoms of allergic conjunctivitis, using the conjunctival allergen challenge model. Methods: This was a single-center, double-masked, randomized, placebo-controlled, contralateral-eye comparison, allergen challenge trial conducted in the United States.

Subjects were randomized to receive ketotifen 0.025% in one eye and placebo in the other. At visits 1 and 2, allergen challenges were performed to determine the allergen concentration eliciting a qualifying reaction for each subject. At the 3 subsequent visits, subjects received 1 drop of **ketotifen** 0.025% **ophthalmic** solution in one eye and vehicle solution as placebo in the other eye 15 min (visit 3), 6 h (visit 4), and 8 h (visit 5) before allergen challenge. The primary efficacy measure was the subject's rating of itching at 3, 7, and 10 min after challenge. Results: Of the 89 subjects randomly assigned to masked trial medication at visit 3, 72 completed the study. At visits 3, 4, and 5, mean itching scores were significantly better for ketotifen-treated eyes at all postchallenge time points, compared with placebo (P<.001). Also at visits 3, 4, and 5, ketotifen was statistically superior to placebo in reducing ocular hyperemia at all postchallenge time points (P<.05). Conclusions: Ketotifen was safe and statistically effective in reducing ocular itching and hyperemia associated with allergic conjunctivitis. Ketotifen's rapid onset of action (within 15 min) and extended duration of action (at least 8 h) make it a valuable treatment for allergic conjunctivitis.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 23 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 14
AN 139:332672 CA
TI Efficacy and safety of ketotifen eye drops as adjunctive therapy to mometasone nasal spray in subjects with seasonal allergic rhinoconjunctivitis
AU Horak, F.; Stuebner, P.; Zieglmayer, R.; McWhirter, C. L.; Gekkieva, M.
CS ENT Clinic, University of Vienna, Vienna, Austria
SO Clinical Drug Investigation (2003), 23(9), 597-604
CODEN: CDINFR; ISSN: 1173-2563
PB Adis International Ltd.
DT Journal
LA English
AB Objective: To compare the efficacy and safety of **ketotifen** 0.025% **ophthalmic** solution (one drop/eye) with placebo as adjunctive therapy to mometasone nasal spray (50 μg/spray, two puffs/nostril) in subjects with seasonal allergic rhinoconjunctivitis (SARC). Study design: Single-center, randomized, double-masked, two-treatment, two-period crossover study. Setting: 8-h allergen challenge in the Vienna Challenge Chamber. Study participants: Subjects were ≥18 yr old, had a ≥2-yr history of SARC, and were sufficiently responsive to allergen challenge. Interventions: During each challenge, subjects received a single dose of mometasone + ketotifen or mometasone + placebo. Main outcome measures and results: 47 subjects were randomized, and 44 completed both treatment sequences. Efficacy was based on mean area under the curve (AUC) values for symptom relief scores over time, with the primary variable being the AUC 4-6 h postdose (AUC4-6) for relief of ocular itching. Between-treatment differences were assessed using anal. of variance. While improvement in ocular itching (AUC4-6) was observed with both treatments, improvement was significantly ($p = 0.014$) better with mometasone + ketotifen vs. mometasone + placebo, as was improvement based on AUC0-6 ($p = 0.009$) and AUC0-2 ($p = 0.006$). Similar trends (in favor of mometasone + ketotifen) were observed for improvements in ocular redness, running nose, sneezing and ocular/nasal composite scores ($p \leq 0.05$). None of the safety findings (slit-lamp biomicroscopy, vital signs, adverse events) were clin. significant. One subject discontinued treatment due to mild pharyngitis. Conclusion: Ketotifen eye drops adjunctive to mometasone nasal spray provided greater relief of both ocular and nasal signs and symptoms than mometasone alone in subjects with SARC.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 24 OF 90 MEDLINE on STN
AN 2003415055 MEDLINE
DN PubMed ID: 12955623
TI [Effectiveness and impact in the quality of life of **ketotifen ophthalmic** solution. Results of zeta study in patients with seasonal allergic conjunctivitis].
Efectividad e impacto en la calidad de vida del colirio de ketotifeno. Resultados del estudio zeta en pacientes con conjuntivitis alergica estacional.
AU Lloves J; Montero Iruzubieta J; Sainz De La Maza Serra M T; Fuster Jensen E; Lladonosa Montull A
CS IOBA (Instituto Universitario de Oftalmologia Aplicada), Valladolid, Espana.
SO Archivos de la Sociedad Espanola de Oftalmologia, (2003 Aug) 78 (8) 433-41.
Journal code: 1304603. ISSN: 0365-6691.
CY Spain
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
LA Spanish
FS Priority Journals
EM 200401
ED Entered STN: 20030905
Last Updated on STN: 20040107
Entered Medline: 20040106
AB PURPOSE: To study the effectiveness of **ketotifen ophthalmic** solution (0.25 mg/ml) in seasonal allergic conjunctivitis (SAC) and the impact on the patient's quality of life. METHODS: A multicentric, longitudinal, prospective study was designed. 284 Spanish ophthalmologists participated recruiting 1145 patients with SAC. After obtaining the informed consent, a drop of **ketotifen ophthalmic** solution was instilled. At the visit, clinical symptoms pre and post-treatment were assessed. The patients answered a questionnaire of quality of life (QOL) pre-treatment and minimum one week after initiating the treatment. The qualitative variables were described by the percentage, and the quantitative were described by the average, median, standard deviation, and maximum and minimum values. The effectiveness (change of intensity of the symptoms) and the quality of life were studied by the Wilcoxon test with a significance level of 5% (alpha = 0.05). RESULTS: Following the instillation of the **ketotifen ophthalmic** solution the intensity of the ocular symptoms (redness, edema, tearing, secretion, photophobia and visual acuity impairment) decreased significantly. Comparing both QOL, we observed a statistically significant reduction of the limitation perceived by the patients in their daily activities, animic state and ocular symptoms. In 0,7% some adverse event was referred, none was serious and only in one case the probable relationship with the drug was specified. CONCLUSION: The results of the ZETA study demonstrate the tolerability and effectiveness of the **ketotifen ophthalmic** solution for all the symptoms of SAC in clinical practice, observing improvement in the quality of life of the patient.

L2 ANSWER 25 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 15
AN 139:127638 CA
TI Onset and duration of action of ketotifen 0.025% and emedastine 0.05% in seasonal allergic conjunctivitis: efficacy after repeated pollen challenges in the Vienna challenge chamber
AU Horak, Friedrich; Stubner, Petra; Zieglmayer, Rene; Kawina, Alexander; Moser, Michael; Lanz, Rene
CS ENT Clinic, University of Vienna, Vienna, Austria
SO Clinical Drug Investigation (2003), 23(5), 329-337
CODEN: CDINFR; ISSN: 1173-2563
PB Adis International Ltd.

DT Journal
LA English
AB The aim of this study was to compare the efficacy, onset and duration of action, and the safety of **ketotifen** fumarate 0.025% **ophthalmic** solution and emedastine difumarate 0.05% ophthalmic solution in subjects with seasonal allergic conjunctivitis (SAC) induced by allergen exposure, using the Vienna Challenge Chamber model. This was a double-masked, randomized, comparative, crossover study conducted at an allergy outpatient clinic in Austria. Subjects with an allergy to grass pollen were exposed to the allergen in a pollen chamber for 4 h, followed by a 3-h break and then a second exposure for 3 h. Study participants were randomized to a treatment sequence (ketotifen followed by emedastine or emedastine followed by ketotifen), receiving 1 drop per eye of ketotifen or emedastine 2 h after the initial allergen exposure in the pollen chamber. Individual and composite ocular, individual and composite nasal, and total (ocular + nasal) symptom complex scores were determined by repeated exposure to allergen 0-2 h and 5-8 h after dosing. Onset of action was defined as the time to the first observation of a 20% reduction from baseline in the composite ocular symptom score. All 37 subjects enrolled completed the study. The median time to onset of action was 15 min for ketotifen and 30 min for emedastine. This difference was significant using the generalized linear model ($p = 0.048$), but not for the log-rank test anal. In the initial 2 h post dose, ketotifen provided significantly greater relief of both composite ocular symptoms ($p = 0.026$) and total symptom complex ($p = 0.014$). Both medications were effective in reducing symptoms 5 to 8 h after dosing. No adverse events were reported for either treatment. In the Vienna Challenge Chamber model, ketotifen and emedastine both effectively alleviated ocular symptoms of SAC after single-dose administration. Ketotifen had a faster onset of action and provided better symptom relief than emedastine during the first 2 h after dosing. The rapid onset of action and symptom control make ketotifen a valuable treatment for SAC.
RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 26 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 16
AN 139:173445 CA
TI Ketotifen fumarate and olopatadine hydrochloride in the treatment of allergic conjunctivitis: A real-world comparison of efficacy and ocular comfort
AU Ganz, Michael; Koll, Elizabeth; Gausche, Jean; Detjen, Paul; Orfan, Nicholas
CS Ganz Allergy and Asthma Center, Racine, WI, USA
SO Advances in Therapy (2003), 20(2), 79-91
CODEN: ADTHE7; ISSN: 0741-238X
PB Health Communications
DT Journal
LA English
AB This 3-wk prospective, randomized, double-masked, parallel-group study compared **ketotifen** fumarate 0.025% **ophthalmic** solution and olopatadine hydrochloride 0.1% ophthalmic solution in 66 patients with seasonal allergic conjunctivitis. The drugs were instilled twice daily. Signs and symptoms were assessed on days 5 (visit 2) and 21 (visit 3). Other efficacy variables were the responder rate (patients with excellent or good global efficacy on days 5 and 21) and patient and investigator ratings of global efficacy. Comfort was evaluated immediately after instillation of the first drop and at each follow-up visit. The frequency of adverse events was the safety assessment. The responder rate was higher with ketotifen than with olopatadine on day 5 (72% vs. 54% for patient assessment, 88% vs. 55% for investigator assessment) and day 21 (91% vs. 55%, 94% vs. 42%). Global efficacy ratings were higher with ketotifen, and severity scores for hyperemia and itching were significantly lower. Both drugs elicited comparable comfort ratings. The most common adverse events were burning/stinging and headache.

RE.CNT 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 27 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:338018 BIOSIS
DN PREV200300338018
TI Specific nasal allergic symptoms: Differentiation in their reduction by the ocular use of **ketotifen** fumarate 0.025% **ophthalmic** solution.
AU Dehning, D. [Reprint Author]
CS Discover Vision Centers, Kansas City, MO, USA
SO Journal of Allergy and Clinical Immunology, (February 2003) Vol. 111, No. 2 Abstract Supplement, pp. S75. print.
Meeting Info.: AAAAI 60th Anniversary Meeting. Denver, CO, USA. March 07-12, 2003. American Academy of Allergy, Asthma and Immunology.
CODEN: JACIBY. ISSN: 0091-6749.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 23 Jul 2003
Last Updated on STN: 23 Jul 2003

L2 ANSWER 28 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:544028 BIOSIS
DN PREV200300539519
TI EFFICACY AND SAFETY OF SINGLE - AND MULTIPLE - DOSE KETOTIFEN FUMARATE 0.025% IN A PEDIATRIC POPULATION.
AU Crampton, J. [Reprint Author]; Gomes, P. J. [Reprint Author]; McWhirter, C. L.; Abelson, M. B.
CS Cornea, Ophthalmic Research Associates, North Andover, MA, USA
SO ARVO Annual Meeting Abstract Search and Program Planner, (2003) Vol. 2003, pp. Abstract No. 3728. cd-rom.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, FL, USA. May 04-08, 2003. Association for Research in Vision and Ophthalmology.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 19 Nov 2003
Last Updated on STN: 19 Nov 2003
AB Purpose: To compare the efficacy (onset and duration of action) and safety of **ketotifen** fumarate 0.025% **ophthalmic** solution with vehicle placebo in pediatric subjects after single and multiple doses. Methods: This was a double-masked, multicenter, fellow-eye, placebo-controlled, conjunctival allergen challenge trial. Eligible subjects (8-16 years old) who produced a qualifying reaction to allergen were randomized to 1 drop of ketotifen in 1 eye and placebo in the fellow eye, followed by allergen challenges at 15 minutes and 8 hours postdose. Subjects who had a qualifying reaction to allergen in the placebo-treated eye and a qualifying response to ketotifen in the active-treated eye following the single dose were re-randomized to multiple-dose treatment. They instilled 1 drop of ketotifen in 1 eye and placebo in the other eye twice daily for 4 weeks. An allergen challenge was conducted 8 hours after the last dose. The primary efficacy assessment was ocular itching at 3, 7, and 10 minutes post-challenge. Other ocular signs and symptoms were assessed at 7, 10, and 15 minutes post-challenge. Results: A total of 105 subjects were evaluable for single-dose efficacy and 55 for multiple-dose efficacy. Ketotifen significantly inhibited ocular itching ($P<0.001$) and composite (conjunctival, ciliary, episcleral) hyperemia, chemosis, and lid swelling (Pltoreq0.031) at nearly all post-challenge timepoints. No drug-related systemic adverse events were reported, and

ocular adverse events were comparable to placebo. Conclusions: **Ketotifen** fumarate 0.025% **ophthalmic** solution is an effective and safe treatment option for children with allergic conjunctivitis.

L2 ANSWER 29 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:514836 BIOSIS
DN PREV200300511979
TI SINGLE - DOSE TOLERABILITY COMPARISON OF TOPICAL KETOTIFEN FUMARATE VS. OLOPATADINE HCL IN ALLERGIC CONJUNCTIVITIS.
AU Patterson, S. [Reprint Author]; Raizman, M. B.; Henderson, M.
CS Clinical Research, Novartis Ophthalmics, Duluth, GA, USA
SO ARVO Annual Meeting Abstract Search and Program Planner, (2003) Vol. 2003, pp. Abstract No. 682. cd-rom.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, FL, USA. May 04-08, 2003. Association for Research in Vision and Ophthalmology.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 5 Nov 2003
Last Updated on STN: 5 Nov 2003
AB Purpose: This study compared the single-dose tolerability and safety of ketotifen fumarate 0.025% (KE) and olopatadine HCl 0.1% (OL) ophthalmic solutions in subjects with allergic conjunctivitis. Methods: Eligible subjects, at least 12 years old, with a history and current diagnosis of allergic conjunctivitis, were randomized to receive a single dose of ketotifen or olopatadine in both eyes. Subjects assessed ocular tolerability as burning/stinging on a 5-point rating scale (0=none; 4=severe) prior to and 1 minute after dosing. Tolerability was separately analyzed for subjects who had burning/stinging at baseline and those who did not. Safety assessments included adverse event reports and slit-lamp examinations. Results: A total of 92 (46 KE, 46 OL) subjects were enrolled and completed the study. Of these, 75 (37 KE, 38 OL) subjects had symptoms of burning/stinging at baseline and 17 (9 KE, 8 OL) subjects did not. Both treatments were well tolerated. In subjects with baseline symptoms, ketotifen and olopatadine markedly decreased burning/stinging from baseline by 0.99 and 0.72 score units, respectively. There were no statistically significant between-treatment differences at baseline or postdose in either group. There were no adverse events reported in this study and no changes in slit-lamp examinations. Conclusions: The tolerability of ketotifen fumarate 0.025% and olopatadine HCl 0.1% ophthalmic solutions was similar in a population of subjects with a history and current diagnosis of allergic conjunctivitis, regardless of whether or not the subjects exhibited eye discomfort prior to treatment.

L2 ANSWER 30 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 17
AN 138:29160 CA
TI Ophthalmic compositions containing a linear polysaccharide
IN Babiole Saunier, Maggy; Bizec, Jean-Claude; Fetz, Andrea; Schoch, Christian
PA Novartis AG, Switz.; Novartis Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002100437	A2	20021219	WO 2002-EP6279	20020607
	WO 2002100437	A3	20030424		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

	EP 1404370	A2	20040407	EP 2002-740697	20020607
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2002010139	A	20040608	BR 2002-10139	20020607
PRAI	EP 2001-113958	A	20010608		
	EP 2001-113959	A	20010608		
	EP 2001-115096	A	20010621		
	EP 2001-115097	A	20010621		
	WO 2002-EP6279	W	20020607		

AB Ophthalmic compns. comprising an ophthalmic drug and a linear polysaccharide compound are useful for topical once-a-day administration to the eye. For example, a stable clear, colorless **ophthalmic** solution was prepared containing **ketotifen** hydrogen fumarate 0.0345%, sodium hyaluronate 0.10%, D-sorbitol 4.50%, cetrimide 0.005%, and water up to 100%. The composition demonstrated an improvement of the bioavailability in conjunctiva, cornea and sclera as compared to Zaditen after single dose application.

L2 ANSWER 31 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 18
AN 138:29159 CA
TI Polymer-based ophthalmic compositions
IN Babiole Saunier, Maggy; Bizec, Jean-Claude; Fetz, Andrea; Schoch, Christian
PA Novartis AG, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002100436	A2	20021219	WO 2002-EP6282	20020607
	WO 2002100436	A3	20030925		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
PRAI	EP 2001-113957	A	20010608		
	EP 2001-113960	A	20010608		

AB The invention is directed to an ophthalmic composition adapted for topical once-a-day administration to the eye comprising an ophthalmic drug, in particular to an ophthalmic composition comprising an ophthalmic drug and at least one polymer selected from one or more of (i) a polyoxyethylene-polyoxypropylene copolymer or block copolymer, and (ii) a crosslinked acrylic acid polymer. For example, a stable **ophthalmic** gel was prepared containing **ketotifen** hydrogen fumarate 0.034%, Poloxamer 407 5.0%, Carbopol 980 0.2%, sorbitol 3.5%, TRIS 0.096%, benzalkonium chloride 0.01%, and water up to 100%. The composition showed a good tolerability in rabbit eye and is effective against seasonal allergic conjunctivitis.

L2 ANSWER 32 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 19
AN 138:29143 CA
TI **Ophthalmic** compositions comprising chitosan and **ketotifen** for the treatment of ocular allergic conditions

IN Wong, Michelle Pik-Han; Sou, Mary; Yen, Shau-Fong; Minick, Kasey Jon; Bizec, Jean-Claude
PA Novartis AG, Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002100376	A1	20021219	WO 2002-EP6280	20020607
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LT, LU, LV, MA, MD, MK, MN, MX, NO, NZ, OM, PH, PL, PT, RO, RU, SE, SG, SI, SK, TJ, TM, TN, TR, TT, UA, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR				
	US 2003031718	A1	20030213	US 2002-164756	20020607
PRAI	US 2001-297068P	P	20010608		

AB Disclosed is a once-a-day **ophthalmic** drug composition, in particular **ketotifen**, comprising a polymer comprising chitosan and a carrier, and a method to treat an ocular allergy comprising administering a once-a-day **ophthalmic ketotifen** composition comprising chitosan to the eye of a mammal. A composition contained ketotifen H fumarate 0.0345%, chitosan 0.5, benzalkonium chloride 0.005, mannitol 4.5% weight/volume Na bicarbonate to pH 6.0, and water for injection to 100%.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 33 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 20
AN 136:123671 CA
TI Ophthalmic formulation of a selective cyclooxygenase-2 inhibitory drug
IN Kararli, Tugrul T.; Bandyopadhyay, Rebanta; Singh, Satish K.; Hawley, Leslie C.
PA Pharmacia & Upjohn Company, USA
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002005815	A1	20020124	WO 2001-US22061	20010712
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 2001075908	A5	20020130	AU 2001-75908	20010712
	US 2002035264	A1	20020321	US 2001-904098	20010712
	EP 1303271	A1	20030423	EP 2001-953462	20010712
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	JP 2004528267	T2	20040916	JP 2002-511747	20010712
PRAI	US 2000-218101P	P	20000713		
	US 2001-279285P	P	20010328		
	US 2001-294838P	P	20010531		
	US 2001-296388P	P	20010606		

WO 2001-US22061 W 20010712
OS MARPAT 136:123671
AB A pharmaceutical composition suitable for topical administration to an eye contains a selective COX-2 inhibitor or nanoparticles of a drug of low water solubility, at a concentration effective for the treatment and/or prophylaxis of a disorder in the eye, and 1 or more ophthalmically acceptable excipients that reduce rate of removal from the eye such that the composition has an effective residence time of 2-24 h. Also provided is a method of treating and/or preventing a disorder in an eye, the method comprising administering to the eye a composition of the invention. Thus, an ophthalmic nanoparticle suspension contained valdecoxib at 2.15 mg/g, 1.2% glycerin, 0.8% EDTA disodium salt, 4.0% Gelcarin GP-379NF, 0.21% SeaSpen PF and 0.82% Povidone.
RE.CNT 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 34 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 21
AN 137:299957 CA
TI **Ophthalmic** compositions containing **ketotifen** fumarate
IN Masuda, Kiyoshi; Tanabe, Akiko
PA Taisho Pharmaceutical Industries Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2002308770	A2	20021023	JP 2001-115054	20010413
PRAI JP 2001-115054		20010413		

AB This invention relates to storage-stable, irritation-free eyedrops comprising ketotifen fumarate (I). The eyedrop solution comprises I, boric acid, and borax and its pH is adjusted to 4.5-8.5 using diluted acids and its osmolarity ratio is adjusted to 0.7-1.1. The solution further contains l-menthol, d-borneol, and/or d-camphor and polyhydric alcs., such as glycerin, propylene glycol, and polyethylene glycol. For example, an eyedrop solution (pH 5.24) contained I 0.069, polysorbate-80 0.15, benzalkonium chlorides 0.01, glycerin 0.1, boric acid 1.18, borax 0.2, l-menthol 0.006, did. HCl solution q.s., and distilled water balance to 100 %.

L2 ANSWER 35 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 22
AN 137:299960 CA
TI Ophthalmic compositions containing bromfenac sodium and vasoconstrictors
IN Okudaira, Ichiro; Ichihara, Takashi; Nakagami, Joji; Aikawa, Katsuyoshi
PA Taisho Pharmaceutical Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2002308764	A2	20021023	JP 2001-298850	20010928
PRAI JP 2001-33009	A	20010209		

AB This invention relates to ophthalmic prepns. for the treatment of conjunctivitis. The compns. comprise bromfenac sodium and vasoconstrictors selected from the group consisting of tetrahydrozoline, naphazoline, phenylephrine, ephedrine, methylephedrine, epinephrine, and salts thereof. An eyedrop solution contained bromfenac sodium hydrate 50 mg, naphazoline hydrochloride 2, diphenhydramine hydrochloride 30 mg, and distilled water 100 mL.

L2 ANSWER 36 OF 90 USPATFULL on STN DUPLICATE 23

AN 2002:275755 USPATFULL
TI Autoclavable pharmaceutical compositions containing a chelating agent
IN Kis, Gyorgy Lajos, Triboltingen, SWITZERLAND
PA Novartis AG, Basel, SWITZERLAND (non-U.S. corporation)
PI US 6468548 B1 20021022
AI US 2000-616151 20000714 (9)
RLI Continuation of Ser. No. WO 1999-EP160, filed on 13 Jan 1999
PRAI EP 1998-810016 19980115
DT Utility
FS GRANTED
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Joynes, Robert M.
LREP Wildman, David E.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 0 Drawing Figure(s); 0 Drawing Page(s)
LN.CNT 389
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention describes an autoclavable ophthalmic composition comprising an ophthalmically effective drug. The invention further relates to a method for stabilizing an ophthalmic drug.

L2 ANSWER 37 OF 90 USPATFULL on STN
AN 2002:323190 USPATFULL
TI Ophthalmic composition
IN Adam, Marcia Johanna, Gisikon, SWITZERLAND
Fetz, Andrea, Wetzikon, SWITZERLAND
Kis, Gyorgy Lajos, Triboltingen, SWITZERLAND
PI US 2002183359 A1 20021205
US 6774137 B2 20040810
AI US 2002-134795 A1 20020429 (10)
RLI Division of Ser. No. US 2000-619349, filed on 19 Jul 2000, PENDING
PRAI EP 1999-114508 19990723
DT Utility
FS APPLICATION
LREP THOMAS HOXIE, NOVARTIS CORPORATION, PATENT AND TRADEMARK DEPT, 564 MORRIS AVENUE, SUMMIT, NJ, 079011027
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 116
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is related to an **ophthalmic** composition comprising **ketotifen** as a pharmaceutically active agent.

L2 ANSWER 38 OF 90 USPATFULL on STN
AN 2002:295205 USPATFULL
TI Autoclavable pharmaceutical compositions containing a chelating agent
IN Kis, Gyorgy Lajos, Triboltingen, SWITZERLAND
Adam, Marcia Johanna, Gisikon, SWITZERLAND
Fetz, Andrea, Wetzikon, SWITZERLAND
PI US 2002165254 A1 20021107
US 6776982 B2 20040817
AI US 2001-16361 A1 20011210 (10)
RLI Division of Ser. No. US 2000-616151, filed on 14 Jul 2000, PENDING
Continuation of Ser. No. WO 1999-EP160, filed on 13 Jan 1999, UNKNOWN
PRAI EP 1998-810016 19980115
DT Utility
FS APPLICATION
LREP THOMAS HOXIE, NOVARTIS CORPORATION, PATENT AND TRADEMARK DEPT, 564 MORRIS AVENUE, SUMMIT, NJ, 079011027
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 376
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Disclosed are **ophthalmic** compositions comprising **ketotifen** and pharmaceutically acceptable salts thereof, as well as methods for making such compositions.

L2 ANSWER 39 OF 90 USPATFULL on STN
AN 2002:192125 USPATFULL
TI Method for treating pharmaceutical compositions
IN Kis, Gyorgy Lajos, Triboltingen, SWITZERLAND
PI US 2002103196 A1 20020801
US 6455547 B2 20020924
AI US 2001-33285 A1 20011221 (10)
RLI Continuation of Ser. No. US 2000-627799, filed on 28 Jul 2000, PENDING
Continuation of Ser. No. WO 1999-EP2221, filed on 31 Mar 1999, UNKNOWN
PRAI EP 1998-106046 19980402
DT Utility
FS APPLICATION
LREP THOMAS HOXIE, NOVARTIS CORPORATION, PATENT AND TRADEMARK DEPT, 564 MORRIS AVENUE, SUMMIT, NJ, 079011027
CLMN Number of Claims: 27
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 479
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides stabilized ophthalmic compositions and methods for stabilizing ophthalmic compositions.

L2 ANSWER 40 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2002:375301 BIOSIS
DN PREV200200375301
TI Use of ophthalmic agent.
AU Trimming, Julian [Inventor, Reprint author]; Fetz, Andrea [Inventor]
CS Forch, Switzerland
ASSIGNEE: Novartis AG, Basel, Switzerland
PI US 6395756 May 28, 2002
SO Official Gazette of the United States Patent and Trademark Office Patents, (May 28, 2002) Vol. 1258, No. 4. http://www.uspto.gov/web/menu/patdata.htm l. e-file.
CODEN: OGUPE7. ISSN: 0098-1133.
DT Patent
LA English
ED Entered STN: 10 Jul 2002
Last Updated on STN: 10 Jul 2002
AB The present invention is related to the use an **ophthalmic** composition comprising **ketotifen** in the preparation of an eye medicament for the treatment allergic conjunctivitis of contact lens wearers.

L2 ANSWER 41 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 24
AN 138:49612 CA
TI A comparison of the relative clinical efficacy of a single dose of **ketotifen** fumarate 0.025% **ophthalmic** solution versus placebo in inhibiting the signs and symptoms of allergic rhinoconjunctivitis as induced by the conjunctival allergen challenge model
AU Crampton, H. Jerome
CS Ophthalmic Research Associates, North Andover, MA, USA
SO Clinical Therapeutics (2002), 24(11), 1800-1808
CODEN: CLTHDG; ISSN: 0149-2918
PB Excerpta Medica, Inc.
DT Journal
LA English

AB Background: **Ketotifen** fumarate 0.025% **ophthalmic** solution is an antiallergic treatment currently available in the United States. It is indicated for the temporary prevention of ocular itching due to allergic conjunctivitis. Objective: The purpose of this study was to determine the relative efficacy of ketotifen when applied topically to the eye, compared with placebo, in the treatment of nasal signs and symptoms of allergic rhinoconjunctivitis as induced by the conjunctival allergen challenge (CAC) model. Methods: This was a randomized, double-blind, parallel-group, single-center clin. study using the CAC model. Patients aged ≥18 yr, able to follow the study instructions, willing to avoid disallowed medications, and having a history of rhinoconjunctivitis and a pos. skin test were eligible. At visit 1, the dose of allergen necessary to achieve a qualifying reaction was determined using bilateral ocular instillation of allergen to eligible patients. At visit 2, the allergen dose determined at visit 1 was confirmed, and all patients attaining a qualifying nasal, reaction continued in the study. At visit 3, each patient was randomized to receive 1 drop of ketotifen bilaterally in the eyes or 1 drop of placebo bilaterally. Fifteen minutes after instillation of the study medication, bilateral CAC was performed. Patients rated nasal symptoms (sneezing, rhinorrhea and postnasal drip, nasal pruritus, palatal pruritus, and nasal congestion) on standardized scales at 10, 20, and 30 min after CAC. Results: Thirty-two patients (16 men, 16 women; mean age, 45 yr [range, 28-70 yr]) were randomized to treatment and completed the study. Nineteen patients received ketotifen and 13 received placebo. Nasal symptom scores in ketotifen-treated patients were statistically and clin. significantly fewer than in those treated with placebo at all time points (mean baseline corrected total nasal score: 10 min, P = 0.010; 20 min, P = 0.025; 30 min, P = 0.006). Conclusion: In this study, topical **ketotifen** fumarate 0.025% **ophthalmic** solution, when dosed ocularly, offered protection against the nasal signs and symptoms of acute allergic rhinoconjunctival reaction as induced by the CAC model.

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 42 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 25
AN 137:119287 CA
TI Effect of levocabastine hydrochloride on allergic conjunctivitis in rats
AU Minami, Kazuhisa; Sugimoto, Yukio; Kamei, Chiaki
CS Dep. Pharmacol., Fac. Pharmaceutical Sci., Okayama Univ., Okayama, 700-8530, Japan
SO Atarashii Ganka (2002), 19(6), 787-791
CODEN: ATGAEX; ISSN: 0910-1810
PB Medikaru Aoi Shuppan
DT Journal
LA Japanese
AB The present study was undertaken to clarify the potency and duration of levocabastine hydrochloride (0.025% Livostine eye drops) ophthalmic solution's effect on histamine- and antigen-induced conjunctivitis in rats, in comparison with **ketotifen** fumarate (0.05% Zaditen **ophthalmic** solution). Levocabastine hydrochloride was found to be more effective and long lasting in inhibiting both histamine- and antigen-induced conjunctivitis than ketotifen fumarate. Simultaneous use of levocabastine hydrochloride and pemirolast (0.1% Alegysal ophthalmic solution) significantly heightens the original activities of both drugs in inhibiting antigen-induced conjunctivitis in rats.

L2 ANSWER 43 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 26
AN 137:406 CA
TI Randomized, double-masked, placebo-controlled comparison of the efficacy of emedastine difumarate 0.05% **ophthalmic** solution and **ketotifen** fumarate 0.025% **ophthalmic** solution in the human conjunctival allergen challenge model
AU D'Arienzo, Peter A.; Leonardi, Andrea; Bensch, George

CS Catholic Medical Center of Brooklyn, Brooklyn, NY, USA
SO Clinical Therapeutics (2002), 24(3), 409-416
CODEN: CLTHDG; ISSN: 0149-2918
PB Excerpta Medica, Inc.
DT Journal
LA English
AB Emedastine difumarate 0.05% **ophthalmic** solution and **ketotifen** fumarate 0.025% **ophthalmic** solution are 2 topical antiallergic agents available in the United States and other countries. Emedastine is indicated for the temporary relief of the signs and symptoms of allergic conjunctivitis. Ketotifen is indicated the temporary relief of ocular itching caused by allergic conjunctivitis. The purpose of this study was to compare the efficacy of these agents in the temporary relief of ocular itching due to allergic conjunctivitis. The 2 agents were compared with each other and with placebo (artificial tears) using the conjunctival allergen challenge (CAC) model. This was a single-center, randomized, double-masked, placebo-controlled study. At visit 1, CAC was performed on eligible subjects to identify the dose required to elicit a pos. allergic reaction. Subjects returned after 7 days for visit 2 to confirm the allergen dose. On day 14 (±3) of the study, enrolled subjects were randomized to 1 of 3 treatment groups: emedastine in 1 eye and placebo in the other, ketotifen in 1 eye and placebo in the other, or emedastine in 1 eye and ketotifen in the other. In 25 subjects, bilateral CAC was performed 5 min after study medication instillation. In a second group of 20 subjects, CAC was performed 15 min after medication instillation. Itching was graded according to a standardized 5-point scale (0 = none to 4 = severe itching) at 3, 5, and 10 min postchallenge. Differences in efficacy scores between treatments and vs. placebo were compared using 2-sample t tests of equal variance. A total of 45 patients (mean age, 41.2 yr) received treatment: 16 received emedastine in 1 eye and ketotifen in the other; 14 received emedastine in 1 eye and placebo in the other; and 15 received ketotifen in 1 eye and placebo in the other. Both emedastine and ketotifen significantly inhibited itching ($P < 0.05$) compared with placebo at all time points after the 5- and 15-min CAC. Mean raw scores for the active treatments were not statistically different. The mean itching efficacy scores were also not statistically different between active treatments. No adverse events were reported in this study. The results of this study suggest that emedastine and ketotifen are not significantly different with respect to anti-itching efficacy in the CAC model of acute allergic conjunctivitis.
RE.CNT 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 44 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 27
AN 139:90589 CA
TI Determination of naphazoline chloride and pheniramine maleate in eye drops by HPLC
AU Wang, Yu
CS Jiangsu Provincial Institute of Pharmaceutic Industry, Nanjing, 210042, Peop. Rep. China
SO Yaowu Fenxi Zazhi (2002), 22(4), 319-321
CODEN: YFZADL; ISSN: 0254-1793
PB Yaowu Fenxi Zazhi Bianji Weiyuanhui
DT Journal
LA Chinese
AB The naphazoline chloride (NAP) and pheniramine maleate (PHM) contents in eye drops were determined by HPLC on Phenomenex partisil 10 ODS column (4.6 mm x 250 mm) with mobile phase A: 0.05 mol L-1 sodium dihydrogen phosphate (pH 3.0 adjusted by phosphoric acid), mobile phase B: acetonitrile for gradient elution. The linearity was between 21.55-344.80 μg mL-1 with r = 0.9998 for PHM and 10.26-61.56 μg mL-1 with r = 0.9993 for NAP, resp. The recovery was 100.4 -102.1% and 101.8-105.0% for PHM and NAP resp.

L2 ANSWER 45 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 28
AN 137:379848 CA
TI Single dose of ketotifen fumarate .025% vs 2 weeks of cromolyn sodium 4% for allergic conjunctivitis
AU Greiner, Jack V.; Michaelson, Clifford; McWhirter, Cecilia L.; Shams, Naveed B. K.
CS Schepens Eye Research Institute and Department of Ophthalmology, Harvard Medical School, Boston, MA, USA
SO Advances in Therapy (2002), 19(4), 185-193
CODEN: ADTHE7; ISSN: 0741-238X
PB Health Communications
DT Journal
LA English
AB This single-masked, contra lateral-eye, active-controlled allergen-challenge study compared ketotifen fumarate .025% and cromolyn sodium 4% ophthalmic solns. in the prevention of ocular itching, tearing, and redness induced by allergen challenge. After a confirmatory conjunctival provocation test (CPT), 56 patients randomly received masked study medication (placebo in one eye, cromolyn in the other eye) four times daily for 2 wk. At visit 3, patients received one drop of ketotifen in the eye previously treated with placebo and cromolyn in the other eye. Ocular comfort was assessed 30 s postinstillation, and a CPT was conducted 15 min and 4 h postinstillation to evaluate ocular itching, tearing, and redness. Forty-seven patients were analyzed for efficacy. At the 15-min and 4-h challenges, ketotifen was superior to cromolyn in preventing itching ($P<.001$) at all assessments and redness (ciliary, conjunctival, and episcleral) ($P\leq.001$) at most assessments. Tearing scores were higher in cromolyn-treated eyes than in ketotifen-treated eyes. Patients reported greater comfort in the ketotifen-treated than in the cromolyn-treated eye ($P = .066$). The most common adverse event was burning/stinging with cromolyn. A single dose of ketotifen was superior to a 2-wk four-times-daily regimen of cromolyn in alleviating symptoms of allergic conjunctivitis in the conjunctival allergen-challenge model.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 46 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 29
AN 137:379847 CA
TI Ocular tolerability and safety of **ketotifen** fumarate **ophthalmic** solution
AU Abelson, Mark B.; Chapin, Matthew J.; Kapik, Barry M.; Shams, Naveed B. K.
CS Schepens Eye Research Institute, Department of Ophthalmology, Harvard Medical School, Boston, MA, USA
SO Advances in Therapy (2002), 19(4), 161-169
CODEN: ADTHE7; ISSN: 0741-238X
PB Health Communications
DT Journal
LA English
AB Ketotifen fumarate, formulated for the treatment of allergic conjunctivitis, is a histamine H1-receptor antagonist, mast cell stabilizer, and eosinophil inhibitor (decreases chemotaxis and activation of eosinophils). In this study, healthy volunteers 3 yr of age or older received **ketotifen** fumarate .025% **ophthalmic** solution ($n = 330$) or placebo ($n = 165$) four times daily for 6 wk. Ketotifen was safe and well tolerated in the adult and pediatric populations, with an incidence of ocular adverse events of 18.2%, compared with 15.2% with placebo. No ocular rebound vasodilation or itching was observed within 48 h after treatment. Ketotifen has a favorable safety and tolerability profile, which may have a pos. impact on compliance, an important aspect of effective symptomatic control of allergic conjunctivitis.
RE.CNT 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 47 OF 90 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN

AN 2002-14835 DRUGU T S
TI Treatment of allergic conjunctivitis with **ketotifen** fumarate **ophthalmic** solution 0.025%: a retrospective analysis in a clinical setting.
AU Ganz M; Hubbard S; Koll E; Orfan N
LO Racine, Wis.; Hagerstown, Md., USA
SO Ann.Allergy Asthma Immunol. (88, No. 1, 113, 2002)
CODEN: ALAIF ISSN: 1081-1206
AV No reprint address.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The effect of topical ketotifen fumarate solution was examined retrospectively in 311 patients with allergic conjunctivitis. Nearly all of the patients reported that ketotifen effectively relieved their itching, tearing, redness and lid swelling. Adverse events included dry eyes, headache, stinging and eye discomfort. Ketotifen fumarate is an extremely efficacious and well tolerated agent in the treatment of allergic conjunctivitis. (conference abstract: 2001 Annual Meeting of the American College of Allergy, Asthma and Immunology, Orlando, Florida, USA).

L2 ANSWER 48 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:142044 BIOSIS
DN PREV200300142044
TI A Comparison of Zaditor(R) (**Ketotifen** Fumarate 0.025% **Ophthalmic** Solution) Versus AlocrilTM (Nedocromil Sodium 2% Ophthalmic Solution) in Preventing Ocular Itching as Induced by the Conjunctival Allergen Challenge Model of Acute Allergic Conjunctivitis.
AU Crampton, J. [Reprint Author]; Slugg, A. P. [Reprint Author]; Minno, G.
CS Ophthalmic Research Associates, Inc., North Andover, MA, USA
SO ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 118. cd-rom.
Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 19 Mar 2003
Last Updated on STN: 9 May 2003
AB Purpose: Zaditor(R) (**Ketotifen** Fumarate 0.025% **Ophthalmic** Solution) and AlocrilTM (Nedocromil Sodium 2% Ophthalmic Solution) are two topical anti-allergic medications with different modes of action and efficacy profiles. Both are indicated for itching. This study compared the efficacy and comfort of these agents. Methods: This was a single-centered, double-masked, randomized, placebo and active controlled conjunctival allergen challenge clinical trial. At Visit 1 (day 0) eligible subjects received increasing concentrations of an allergen in both eyes every 10 minutes until a sufficient reaction was elicited. Qualified subjects returned for Visit 2 (day 7) and the allergen dose that elicited a reaction at visit 1 was instilled and the subjects evaluated their itching every 30 sec for 20 min. Those who responded with 2.0 itching bilaterally at 6/40 time points qualified for Visit 3. At Visit 3 (day21) qualified subjects (n=59) were treated at random with either Zaditor(R), AlocrilTM or Placebo in each eye. Five (5) minutes later the allergen dose that confirmed a reproducible response at Visit 2 was instilled bilaterally. Subjects evaluated their ocular itching every 30 seconds for 20 minutes, then chose which therapy they preferred. At Visit 4 (day 35) subjects were treated with the same study medication used at Visit 3. Twelve (12) hours later the allergen used at visits 1, 2, and 3 was administered bilaterally. Subjects evaluated their ocular itching every 30 seconds for 20 minutes, then chose which therapy

they preferred. Results: Five (5) minutes and twelve (12) hours after instillation, Zaditor(R) treated eyes experienced significantly ($p<0.05$) less ocular itching induced by CAC compared to both AlocrilTM and Placebo treated eyes. AlocrilTM treated eyes showed no statistical or clinical difference from Placebo. Zaditor(R) treated eyes were statistically more comfortable ($P<0.05$) than AlocrilTM treated eyes at 1, 2, 5 and 10 minutes after instillation and they showed no difference from Placebo. Based on comfort and subjective efficacy, Zaditor(R) treated eyes (60%) were preferred twice as much as AlocrilTM or Placebo treated eyes (21%, 19%). Conclusion: Zaditor(R) was determined to be significantly more comfortable and effective than AlocrilTM 5 minutes and 12 hours after administration.

L2 ANSWER 49 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2003:142043 BIOSIS
DN PREV200300142043
TI Comparison of a Single Dose of Zaditor(R) (Ketotifen Fumarate 0.025%) to a Two-Week Regimen of Cromolyn Sodium 4% in Subjects with Allergic Conjunctivitis.
AU Greiner, J. V. [Reprint Author]; Gomes, P. J.; Minno, G.
CS Immunology, Schepens Eye Research Inst, Boston, MA, USA
SO ARVO Annual Meeting Abstract Search and Program Planner, (2002) Vol. 2002, pp. Abstract No. 117. cd-rom.
Meeting Info.: Annual Meeting of the Association For Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. May 05-10, 2002.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 19 Mar 2003
Last Updated on STN: 19 Mar 2003
AB Purpose: Zaditor(R) (**Ketotifen** Fumarate 0.025% **Ophthalmic** Solution) and Cromolyn Sodium 4% Ophthalmic Solution are two topical anti-allergic medications with different modes of action and efficacy profiles. Zaditor(R) is indicated for the temporary prevention of itching of the eye due to allergic conjunctivitis. Although indicated in the US for the treatment of VKC, vernal conjunctivitis, and vernal keratitis, Cromolyn is widely used in the management of seasonal allergic conjunctivitis. This study compared the efficacy of these therapies. Method:This was a single-centered, double-masked, randomized, active controlled conjunctival allergen challenge (CAC) clinical trial. At Visit 1 (Day 0) consent was obtained, an ophthalmic exam was performed and increasing concentrations of allergen was instilled bilaterally every 10 minutes to elicit 2.0 ocular itching and hyperemia OU (0-4). Qualified subjects, returned for Visit 2 (Day 7) and the allergen dose that elicited 2.0 itching and hyperemia OU at Visit 1 was instilled bilaterally. Itching was evaluated 7 min after instillation. Hyperemia was evaluated 7 and 15 min after instillation. Qualified subjects (n=59) were given one bottle of masked Cromolyn to instill in one eye and one bottle of masked Placebo in the other eye QID for 14 days. At Visit 3 (Day 21) one drop of Zaditor(R) was placed in the eyes that had received Placebo QID and one drop of Cromolyn was placed in the QID Cromolyn treated eyes. Fifteen (15) minutes later the allergen dose from Visit 2 was instilled bilaterally. Itching was evaluated 7 min after instillation. Hyperemia was evaluated 7 and 15 min after instillation. Four (4) hours after instillation of Zaditor(R) and Cromolyn allergen was again administered bilaterally. Itching was evaluated 7 min after instillation. Hyperemia was evaluated 7 and 15 min after instillation. Results: Mean efficacy scores were evaluated for ocular itching and ocular hyperemia. At fifteen (15) minutes and four (4) hours after instillation Zaditor(R) treated eyes showed less ocular itching (-1.64, $p<0.001$; -0.81, $p<0.001$) compared to Cromolyn treated eyes. Zaditor(R) treated eyes also showed less conjunctival hyperemia compared to Cromolyn fifteen (15) minutes and four (4) hours after instillation. Conclusion: A single dose of Zaditor(R) (**Ketotifen** Fumarate 0.025% **Ophthalmic** Solution) is

superior to a 2 week QID treatment of Cromolyn Sodium 4% in preventing the signs and symptoms of allergic conjunctivitis.

L2 ANSWER 50 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 30
AN 134:136713 CA
TI **Ophthalmic** composition containing **ketotifen** salt
IN Adam, Marcia Johanna; Fetz, Andrea; Kis, Gyorgy Lajos
PA Novartis A.-G., Switz.; Novartis-Erfindungen
SO PCT Int. Appl., 6 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2001007049	A2	20010201	WO 2000-EP7030	20000721
	WO 2001007049	A3	20010329		
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6777429	B1	20040817	US 2000-619349	20000719
	BR 2000012696	A	20020409	BR 2000-12696	20000721
	EP 1198223	A2	20020424	EP 2000-953080	20000721
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
	JP 2003505419	T2	20030212	JP 2001-511933	20000721
	EE 200200040	A	20030415	EE 2002-40	20000721
	NZ 516108	A	20040430	NZ 2000-516108	20000721
	AU 775832	B2	20040819	AU 2000-65655	20000721
	ZA 2002000425	A	20020829	ZA 2002-425	20020117
	NO 2002000319	A	20020121	NO 2002-319	20020121
	US 2002183359	A1	20021205	US 2002-134795	20020429
	US 6774137	B2	20040810		
PRAI	EP 1999-114508	A	19990723		
	AU 1999-26169	A3	19990113		
	US 2000-619349	A3	20000719		
	WO 2000-EP7030	W	20000721		

AB An **ophthalmic** composition comprises **ketotifen** as a pharmaceutically active agent. A composition contains ketotifen fumarate 0.25, benzalkonium chloride 0.10, glycerol 21.25 mg, SaOH 1N 0.75 mg and water for injection ad 1.0 mL.

L2 ANSWER 51 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 31
AN 135:82026 CA
TI **Ophthalmic** compositions containing **ketotifen**
IN Trimming, Julian; Fetz, Andrea
PA Switz.
SO U.S. Pat. Appl. Publ., 3 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001006968	A1	20010705	US 2000-741245	20001220
	US 6395756	B2	20020528		
	WO 2001047521	A1	20010705	WO 2000-EP13123	20001221
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,				

CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1244449 A1 20021002 EP 2000-991623 20001221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
JP 2003518498 T2 20030610 JP 2001-548115 20001221
PRAI EP 1999-125739 A 19991223
WO 2000-EP13123 W 20001221

AB The present invention is related to the use of an **ophthalmic** composition comprising **ketotifen** for the treatment allergic conjunctivitis of contact lens wearers. Thus, a multidose unit composition contained Ketotifen fumarate 0.25, benzalkonium chloride 0.10, and 1N NaOH 0.75 mg and water for injection to 1 mL.

L2 ANSWER 52 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 32
AN 135:97453 CA
TI Ophthalmic compositions containing allergy inhibitors, antihistaminics, vasoconstrictors, and terpenoids
IN Ishii, Reiko; Koide, Misao
PA Lion Corp., Japan
SO Jpn. Kokai Tokkyo Koho, 11 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2001187728	A2	20010710	JP 1999-377142	19991228
PRAI JP 1999-377142		19991228		

AB Ophthalmic compns., which have reduced irritating action and rapidly relieve pruritus and congestion in allergic conjunctivitis, etc., contain antiallergic agents, antihistaminics, vasoconstrictors, and terpenoids. An eye drop (pH 5.5) containing Na cromoglycate 1.0, chlorpheniramine maleate 0.02, tetrahydrozoline hydrochloride 0.03, l-menthol 0.01, propylene glycol 1.0, benzalkonium chloride 0.002, borax 0.2, boric acid 1.0, Na edetate 0.01%, pH controller, and H2O balance was prepared Effect of the eye drop on allergic patients was also evaluated.

L2 ANSWER 53 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 33
AN 135:37171 CA
TI Antiallergic ophthalmic preparations for soft contact lens wearers and method to sustain the effect
IN Ishii, Reiko; Koide, Misao
PA Lion Corp., Japan
SO Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2001158750	A2	20010612	JP 1999-343162	19991202
PRAI JP 1999-343162		19991202		

AB The compns., which suppress allergy symptoms due to wearing of soft contact lenses, contain allergy inhibitors. Antiallergic effect of the compns. are sustained by adding polymers and/or nonionic surfactants. Antipruritic effect of an eye drop containing Na cromoglycate and Me cellulose on allergy of eyes wearing soft contact lenses sustained continued

≥60 min.

L2 ANSWER 54 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 34
AN 134:256908 CA
TI Ophthalmic pharmaceuticals containing allergy inhibitors, antihistamines, and terpenoids
IN Suzuki, Takahiro
PA Lion Corp., Japan
SO Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 2001097865	A2	20010410	JP 1999-312799	19990929
PRAI JP 1999-312799		19990929		

AB This invention relates to ophthalmic compns. comprising allergy inhibitors, antihistamines, and terpenoids for fast relief from itching. The allergy inhibitors are selected from the group consisting of amlexanox, tranilast, pemirolast potassium, and ketotifen fumarate; the antihistamines are selected from the group consisting of chlorpheniramine maleate and diphenhydramine hydrochloride; and the terpenoids are selected from menthol, camphor, borneol, geraniol, cineole, linalool, Eucalyptus oil, bergamot oil, fennel oil, and rose oil. For example, an eyedrop solution contained amlexanox 0.25, chlorpheniramine maleate 0.0015, l-menthol 0.01, propylene glycol 1, benzalkonium chloride 0.002, borax 0.2, boric acid 1.0, Na edetate 0.01 g, and distilled water 100 mL.

L2 ANSWER 55 OF 90 USPATFULL on STN
AN 2001:131341 USPATFULL
TI Pheniramine-containing compositions and method for treating allergic responses
IN Jonasse, Matthew S., Sodus, NY, United States
Smerbeck, Richard V., Pittsford, NY, United States
PA Bausch & Lomb Incorporated, Rochester, NY, United States (U.S. corporation)
PI US 6274626 B1 20010814
AI US 1998-219165 19981222 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Fay, Zohreh
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 453
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention relates to compositions comprising pheniramine. In particular, it has been found that pheniramine in combination with n effective amount of a povidone provides improved comfort and reduces the symptoms of dryness compared to compositions with pheniramine alone.

L2 ANSWER 56 OF 90 WPIDS COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2002-090426 [12] WPIDS
DNC C2002-027977
TI New 1,3-bis-(substituted phenyl)-2-propen-1-one compounds are vascular adhesion molecule (VCAM-1) inhibitors, for treating e.g. inflammation, arthritis, asthma, atherosclerosis and autoimmune diseases.
DC B05
IN HOONG, L K; MENG, C Q; NI, L; SIKORSKI, J A
PA (ATHE-N) ATHEROGENICS INC
CYC 97
PI WO 2001098291 A2 20011227 (200212)* EN 219
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK
DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR
KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU
SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001068610 A 20020102 (200230)
BR 2001011889 A 20030624 (200343)
EP 1330448 A2 20030730 (200350) EN
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
RO SE SI TR
KR 2003031500 A 20030421 (200353)
US 6608101 B1 20030819 (200356)
CN 1447804 A 20031008 (200403)
JP 2004501147 W 20040115 (200410) 390

ADT WO 2001098291 A2 WO 2001-US19720 20010620; AU 2001068610 A AU 2001-68610 20010620; BR 2001011889 A BR 2001-11889 20010620, WO 2001-US19720 20010620; EP 1330448 A2 EP 2001-946583 20010620, WO 2001-US19720 20010620; KR 2003031500 A KR 2002-717448 20021220; US 6608101 B1 Provisional US 2000-212769P 20000620, Provisional US 2000-255934P 20001215, US 2001-886348 20010620; CN 1447804 A CN 2001-814390 20010620; JP 2004501147 W WO 2001-US19720 20010620, JP 2002-504247 20010620

FDT AU 2001068610 A Based on WO 2001098291; BR 2001011889 A Based on WO 2001098291; EP 1330448 A2 Based on WO 2001098291; JP 2004501147 W Based on WO 2001098291

PRAI US 2000-255934P 20001215; US 2000-212769P 20000620;
US 2001-886348 20010620

AB WO 200198291 A UPAB: 20020906

NOVELTY - 1,3-Bis-(substituted phenyl)-2-propen-1-one compounds (I) are new.

DETAILED DESCRIPTION - 1,3-Bis-(substituted phenyl)-2-propen-1-one compounds of formula (I) and their salts are new.

R22, R23 = H or 1-4C alkyl;

R2-R6, R'2-R'6 = H, alkyl, carbocycle, aryl, heteroaryl, heterocycle, cycloalkyl, alkoxy, aryloxy, arylalkoxy, heteroaryloxy, heteroarylalkoxy, alkylthio, alkylamino, aminoalkyl, haloalkylthio, acyl, haloalkyl, aryloxy, amido, acylamino, amino, dialkylamino, aminodialkyl, trifluoroalkoxy, alkylsulfonyl, haloalkylsulfonyl, aminocarbonyl, alkenyl, alkynyl, halo, OH, SH, CN, NO2, sulfonic acid, sulfonate, sulfate, sulfinic acid, sulfenic acid, sulfamide, sulfonamide, sulfoxide, metal sulfinate, phosphate, phosphonate, metal phosphonate, phosphinate, alditol, carbohydrate, amino acid, OC(R1)2COOH, SC(R1)2COOH, NHC(R1)2COOH, COR7, COOR1, polyoxyalkylene, polylol alkyl, oxyalkylamino, alkylcarbonylalkyl, lower alkyl-S(O)-lower alkyl, lower alkyl-S(O)2-lower alkyl, or hydroxyalkyl, aralkoxy, heteroaryl lower alkoxy, heterocyclo lower alkoxy, heteroaryloxy, heterocycleoxy, aralkyl lower thioalkyl, heteroaralkyl lower thioalkyl, heterocycloalkyl lower thioalkyl, heteroaryl lower alkyl, heterocyclo lower alkyl, heteroarylthio lower alkyl, heterocyclothio lower alkyl, heteroarylamino lower alkyl, heterocycloamino lower alkyl, arylsulfinyl lower alkyl, arylsulfonyl lower alkyl (all optionally substituted by a moiety that does not affect biological properties), lower alkylcarbonyl-lower alkyl, carboxy lower alkyl, lower alkylamino-lower alkyl, N,N-di(lower alkyl)amino lower alkyl, -C(O)CH2CH2COO-M+, -SO3M+, lower alkyl-O-R;

R = PO2(OH)-M+, PO3(OH)-M+ or SO3M+;

M+ = pharmaceutically acceptable cation;

R1 = H, lower alkyl, optionally substituted carbocycle, aryl, heteroaryl, heterocycle, alkylaryl, alkylheteroaryl or alkylheterocycle;

R7 = optionally substituted alkyl, alkenyl, alkynyl, aryl, carbocycle, heteroaryl, heterocycle, alkylaryl, alkylheteroaryl or alkylheterocycle;

R22+R6, R23+R6 = bridged carbocycle, aryl, heterocycle or heteroaromatic; and

R2+R3, R3+R4, R4+R5, R5+R6, R'2+R'3, R'3+R'4, R'4+R'5, R'5+R'6 = carbocycle, cycloalkenyl, cycloalkylcarbonyl, cycloalkenylcarbonyl, aryl,

heterocycle, heteroaromatic (all optionally substituted) or alkylenedioxy (ring optionally including carbonyl, cyclic ester, amide, amine, sulfonate or phosphonate;

provided that at least 1 R2-R6, R'2-R6 or R2+R3, R3+R4, R4+R5, R5+R6, R'2+R'3, R'3+R'4, R'4+R'5, R'5+R' is a heterocycle or heteroaromatic; and at least 1 R2-R6, R'2-R6 is not H.

ACTIVITY - Antiinflammatory; Antiarthritic; Antiasthmatic; Dermatological; Antipsoriatic; Immunosuppressive; Neuroprotective; Antiarteriosclerotic; Vasotropic; Cardiant; Antianginal; Antirheumatic; Gastrointestinal; Antidiabetic; Opthalmological; Nephrotropic; Antiallergic.

MECHANISM OF ACTION - Vascular adhesion molecule-1 (VCAM-1) inhibitor.

In an in vitro VCAM-1 assay, 3-(5-(benzo(b)thien-2-yl)-2,4-dimethoxyphenyl)-1-(4-carboxymethoxy-3,5-dimethoxyphenyl)-2-propen-1-one sodium salt (Ia) displayed an IC50 value of 0.7 micro M.

USE - Compounds (I) are useful for treating VCAM-1 mediated disorders e.g. arthritis, asthma, dermatitis, psoriasis, cystic fibrosis, transplant rejection, chronic solid organ rejection, multiple sclerosis, atherosclerosis, post-angioplasty restenosis, coronary artery disease, angina, small artery disease, systemic lupus erythematosus, Crohn's disease, rheumatoid arthritis, inflammatory bowel disease, autoimmune diabetes, diabetic retinopathy, rhinitis, ischemia-reperfusion injury, chronic obstructive pulmonary disease (COPD), glomerulonephritis, Graves' disease, gastrointestinal allergies and conjunctivitis (all claimed). Dwg.0/9

L2 ANSWER 57 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:306522 BIOSIS
DN PREV200100306522
TI Two randomized, double-masked, placebo-controlled single-dose efficacy and safety studies of ketotifen fumarate 0.025%.
AU Reaves, A. T. [Reprint author]; Abelson, M. B.; Mundorf, T. K.; Lonsdale, J.; Casey, R.; Parver, L. M.; Brown, A. L. [Reprint author]; Kapik, B. M. [Reprint author]; Patterson, S. E. [Reprint author]; Shams, N. B. K. [Reprint author]
CS CIBA Vision, Duluth, GA, USA
SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S909. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

L2 ANSWER 58 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:306519 BIOSIS
DN PREV200100306519
TI A randomized, double-masked, single-dose, crossover efficacy and safety comparison of ketotifen fumarate 0.025% and emedastine 0.05%.
AU Lanz, R. [Reprint author]; Horak, F.; Stuebner, P.; Zieglmayer, R.; Schwenninger, C. [Reprint author]; Patterson, S. E.; Shams, N. B. K.
CS CIBA Vision AG, Bulach, Switzerland
SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S909. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

L2 ANSWER 59 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:306515 BIOSIS
DN PREV200100306515
TI A randomized, double-masked, placebo-controlled, efficacy and safety study of ketotifen fumarate 0.025%.
AU Greiner, J. V. [Reprint author]; Abelson, M. B. [Reprint author]; DuBiner, H.; Lanz, R.; Fetz, A. B.; Brown, A.; Kapik, B. M.; Truett, K. R.; Patterson, S.; Shams, N. B. K.
CS Immunology, Schepens Eye Research Inst, Boston, MA, USA
SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S908. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 27 Jun 2001
Last Updated on STN: 19 Feb 2002

L2 ANSWER 60 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2002:413856 BIOSIS
DN PREV200200413856
TI Evaluation of spontaneous contamination of ocular medications.
AU Marchese, A.; Bozzolasco, M.; Gualco, L.; Schito, G. C.; Debbia, E. A. [Reprint author]
CS Institute of Microbiology 'C.A. Romanzi', University of Genoa School of Medicine, Largo Rosanna Benzi, 10, I-16132, Genova, Italy
eugenio.debbia@aleph.it
SO Chemotherapy, (July-August, 2001) Vol. 47, No. 4, pp. 304-308. print.
CODEN: CHTHBK. ISSN: 0009-3157.
DT Article
LA English
ED Entered STN: 31 Jul 2002
Last Updated on STN: 23 Sep 2002
AB Background: In order to evaluate whether single-dose ophthalmic preparations in 0.5-ml containers can safely be used within 24 h after the first opening, eigth different sterile ocular medications containing timolol, jaluronic acid, diclofenac, ketotifen, pilocarpine, formocortal, formocortal-gentamycin, and tetryzoline-feniramine (Farmigea, Italy) were opened and tested for spontaneous bacterial contamination after exposure to air. Methods: Samples (10 mul) were collected from exposed ophthalmic preparations after 0, 2, 4, 8 and 24 h. Results: No viable microorganisms were detected during and at the end of the evaluation period. In order to assess whether the resident or pathogenic ocular bacterial population due to repeated handling might contaminate the medications, about 105 cells of different species (Staphylococcus aureus, coagulase-negative staphylococci, Streptococcus pneumoniae, Streptococcus spp., Corynebacterium spp., Pseudomonas aeruginosa, Neisseria spp., Acinetobacter spp., Haemophilus influenzae, Escherichia coli and Candida albicans) were added to the containers and incubated at 37degreeC or at room temperature. Samples were collected and the number of viable bacteria was estimated. The antibacterial effect of the ophthalmic compounds varied depending on the species considered. Tetryzoline-feniramine, pilocarpine, ketotifen and formocortal-gentamycin exhibited a frank bactericidal activity (<100 survivors after 18-24 h of exposure) against the great majority of the species tested. Conclusion: These results indicate that the risk of spontaneous contamination of ophthalmic preparations after their first opening is low, and that all preparations tested exhibit an aspecific antibacterial activity. As a consequence, the safe usage of these ocular medications could be extended from the recommended 3 h to at least 24 h after the first usage.

L2 ANSWER 61 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:317807 BIOSIS
DN PREV200100317807
TI Ketotifen Fumarate treatment of superior limbic keratoconjunctivitis.
AU Madani-Becker, J. [Reprint author]; Udell, I. J. [Reprint author]; Guidera, A. C. [Reprint author]
CS Department of Ophthalmology, Long Island Jewish Medical Center, New Hyde Park, NY, USA
SO IOVS, (March 15, 2001) Vol. 42, No. 4, pp. S265. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. April 29-May 04, 2001.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 4 Jul 2001
Last Updated on STN: 19 Feb 2002

L2 ANSWER 62 OF 90 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2001-23695 DRUGU T P
TI Efficacy and safety evaluations of **ketotifen** fumarate **ophthalmic** solution (0.025%) in clinical studies.
AU Zhu J; Mundorf T; Abelson M; Brown A; Shams N
LO Duluth, Ga., USA
SO Ann.Allergy Asthma Immunol. (86, No. 1, 114, 2001)
CODEN: ALAIF ISSN: 1081-1206
AV No reprint address.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The optimal concentration of **ketotifen** fumarate **ophthalmic** solution was determined in 4 separate double-masked, randomized, placebo-controlled trials in healthy pediatric and adult volunteers and in hypersensitive individuals in an antigen challenge model. Ketotifen fumarate provided clinically and statistically significant efficacy in prevention of itching in the antigen challenge model. Ketotifen (0.025% to 0.15%) was safe and effective after a single dose in relieving the signs and symptoms of induced allergic conjunctivitis in sensitive individuals. Ketotifen was safe and well-tolerated when instilled q.i.d. for 6 wk in volunteers with normal ocular health, including children as young as 3 yr old. (conference abstract: 2000 Annual Meeting of the American College of Allergy, Asthma and Immunology, Seattle, Washington, USA).

L2 ANSWER 63 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 35
AN 136:139741 CA
TI Preparation of eye drops of ketotifen fumarate
AU Zhou, Lixin; Yang, Bin
CS Jiangsu Prov. Institute of Pharmacy, Nanjing, 210009, Peop. Rep. China
SO Guangdong Yaoxueyuan Xuebao (2001), 17(1), 38-39
CODEN: GYXUF8
PB Guangdong Yaoxueyuan
DT Journal
LA Chinese
AB Eye drops of ketotifen fumarate were prepared from the drug 6.9, NaCl 8.5 and H3BO3 11.0 g, 5% benzalkonium bromide 1, borax qs and water to 1000 mL. The content of ketotifen fumarate in eye drops was determined by spectrophotometry at 301 nm. The stability and toxicity were studied.

L2 ANSWER 64 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 36
AN 134:61558 CA
TI Topical ophthalmic mast cell stabilizers for treating allergic eye diseases

IN Graff, Gustav; Yanni, John M.
PA Alcon Laboratories, Inc., USA
SO PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000078396	A2	20001228	WO 2000-US6890	20000316
	WO 2000078396	A3	20010816		
	W: AU, CA, JP				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 2000038883	A5	20010109	AU 2000-38883	20000316
	AU 770975	B2	20040311		
	EP 1187617	A2	20020320	EP 2000-917998	20000316
	EP 1187617	B1	20040303		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	US 6420399	B1	20020716	US 2000-527401	20000316
	JP 2003502393	T2	20030121	JP 2001-504456	20000316
	AT 260660	E	20040315	AT 2000-917998	20000316
	PT 1187617	T	20040630	PT 2000-917998	20000316
PRAI	US 1999-139945P	P	19990618		
	US 1999-158177P	P	19991007		
	WO 2000-US6890	W	20000316		

AB Topical ophthalmic anti-allergy drugs are identified by the extent of their interaction with a phospholipid model membrane. Disclosed are topically administrable ophthalmic formulations containing amphipathic anti-allergy compds. at concns. such that the drugs have Surface Activity Ratings 2-11. The amphipathic antiallergy drugs of the present invention preferably possess antihistamine activity. The amphipathic antiallergy drugs of the present invention exclude olopatadine, ketotifen, emedastine, pheniramine, pyrilamine, cromolyn, nedocromil, and levocabastine.

L2 ANSWER 65 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 37
AN 133:64000 CA
TI **Ophthalmic** compositions comprising **pheniramine** and povidone
IN Jonasse, Matthew S.; Smerbeck, Richard V.
PA Bausch & Lomb Incorporated, USA
SO PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000037080	A1	20000629	WO 1999-US28147	19991129
	W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MW, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	US 6274626	B1	20010814	US 1998-219165	19981222
PRAI	US 1998-219165	A	19981222		

AB This invention relates to **ophthalmic** compns. comprising **pheniramine**. In particular, it has been found that pheniramine in combination with povidone provides improved comfort and reduces allergic symptoms and symptoms of dryness compared to compns. with pheniramine alone. An **ophthalmic** solution contained **pheniramine**

maleate 0.45, PVP K30 2, NaCl 0.35, KCl 0.3, Na borate 0.45, sorbic acid 0.1, boric acid q.s., EDTA 0.05, and purified water q.s. to 100 %.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 66 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 38
AN 133:63999 CA
TI Ophtalmic compositions comprising pheniramine and a demulcent such as PVP
IN Abelson, Mark B.; Jonasse, Matthew S.; Smerbeck, Richard V.
PA Bausch & Lomb Incorporated, USA
SO PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2000037079	A1	20000629	WO 1999-US30950	19991222

W: AE, AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MW, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI US 1998-219326 A 19981222
AB This invention relates to compns. comprising pheniramine. In particular, it has been found that relatively higher concns. of pheniramine, when employed in combination with an effective amount of a demulcent such as povidone to maintain comfort, provide an improved response to allergic conditions, including the alleviation of redness comparable to compns. with conventional vasoconstrictors. The present composition has also been found to reduce the symptoms of burning and dryness compared to compns. with pheniramine alone. An eye drop contained pheniramine maleate 0.45, PVP K30 2, NaCl 0.35, KCl 0.3, Na borate 0.45, sorbic acid 0.1, EDTA 0.05, and purified water q.s. to 100 %.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 67 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2000:273101 BIOSIS
DN PREV200000273101
TI Evaluation of the efficacy and safety of ketotifen fumarate in the allergen challenge model.
AU Gomes, P. J. [Reprint author]; Welch, D. L. [Reprint author]; Abelson, M. B.
CS Ophthalmic Research Associates, North Andover, MA, USA
SO IOVS, (March 15, 2000) Vol. 41, No. 4, pp. S926. print.
Meeting Info.: Annual Meeting of the Association in Vision and Opthalmology. Fort Lauderlade, Florida, USA. April 30-May 05, 2000. Association for Research in Vision and Ophthalmology.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 30 Jun 2000
Last Updated on STN: 5 Jan 2002

L2 ANSWER 68 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 39
AN 134:80623 CA
TI A comparison of the relative efficacy and clinical performance of olopatadine hydrochloride 0.1% **ophthalmic** solution and **ketotifen** fumarate 0.025% **ophthalmic** solution in the

conjunctival antigen challenge model
AU Berdy, Gregg J.; Spangler, Dennis L.; Bensch, George; Berdy, Susan S.; Brusatti, Robert C.
CS Department of Ophthalmology, Washington University School of Medicine, St. Louis, MO, USA
SO Clinical Therapeutics (2000), 22(7), 826-833
CODEN: CLTHDG; ISSN: 0149-2918
PB Excerpta Medica, Inc.
DT Journal
LA English
AB The purpose of this study was to compare the relative efficacy and clin. performance of olopatadine hydrochloride 0.1% **ophthalmic** solution and **ketotifen** fumarate 0.025% **ophthalmic** solution in the conjunctival antigen challenge model. This was a prospective, randomized, double-masked, contralaterally controlled, single-center, antigen challenge study. Of the 53 subjects screened, 32 were enrolled and completed the study. The study comprised 3 visits. Primary efficacy variables were ocular itching (assessed at visits 2 and 3) and subject satisfaction (assessed at visit 3). Tolerability variables were slit-lamp findings (all visits), visual acuity (all visits), ocular comfort after drug instillation (visit 3), and adverse events (visits 2 and 3). At visit 1, the antigen concentration that elicited a pos. ocular allergic response was determined, and this concentration was confirmed at visit 2. Subjects graded itching on a 5-point scale at 3, 5, and 10 min postchallenge. The scores from this visit were used as baseline scores and compared with scores from visit 3 to determine drug efficacy. At visit 3, subjects were randomly assigned to 2 treatment groups. Group A received 1 drop of olopatadine in the right eye and 1 drop of ketotifen in the left eye. Group B received 1 drop of olopatadine in the left eye and 1 drop of ketotifen in the right eye. Following drug instillation, the subjects assessed the comfort level in each eye. Twelve hours after instillation, subjects were challenged with the antigen concentration that elicited a pos. response at the previous visits. Itching was subjectively graded at 3, 5, and 10 min postchallenge. Subjects were asked to choose which therapy they were more satisfied with. Twelve hours after administration, efficacy scores for olopatadine were significantly higher than those for ketotifen at 3 and 5 min postchallenge (1.84 and 1.75 vs 1.25 and 1.34). Olopatadine-treated eyes were rated significantly more comfortable than those treated with ketotifen immediately after drug instillation (1.25 vs 2.09; $P < 0.05$) and 12 h later, as measured by patient ratings of ocular comfort. Of the 22 subjects who had a preference, 16 (73%) were more satisfied with olopatadine than with ketotifen. Olopatadine is more effective than ketotifen in reducing the itching associated with allergic conjunctivitis in the antigen challenge model. Olopatadine caused less ocular discomfort than ketotifen and was preferred by .apprx.3 times as many patients as was ketotifen.
RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 69 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2000:259611 BIOSIS
DN PREV200000259611
TI Ketotifen fumarate exerts multiple effects in the allergic cascade in the eye.
AU Schoch, C. [Reprint author]; Leuschner, J.
CS Ophtha R+D Basel, Ciba Vision AG, Basel, Switzerland
SO IOVS, (March 15, 2000) Vol. 41, No. 4, pp. S368. print.
Meeting Info.: Annual Meeting of the Association in Vision and Opthalmology. Fort Lauderlade, Florida, USA. April 30-May 05, 2000. Association for Research in Vision and Ophthalmology.
DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 21 Jun 2000
Last Updated on STN: 5 Jan 2002

L2 ANSWER 70 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 40
AN 133:53375 CA
TI Inhibitory effects of ketotifen on scratching behavior in mice and guinea pigs
AU Inagaki, Naoki; Nagao, Masashi; Nagai, Hiroichi; Masatomo, Kato; Miyaji, Suguru; Nakata, katsuhiko
CS Department of Pharmacology, Gifu Pharmaceutical University, Japan
SO Arerugi, Men'eki (2000), 7(2), 256-260
CODEN: ARMEFS; ISSN: 1344-6932
PB Iyaku Janarusha
DT Journal
LA Japanese
AB Effects of ketotifen on scratching behaviors in mice and guinea pigs caused by immediate hypersensitivity reactions were investigated. Passive cutaneous anaphylaxis was evoked in the back skin of ICR mice, and the scratching behavior associated with the cutaneous reaction was observed Ketotifen given i.p. inhibited the scratching behavior significantly. Exptl. allergic conjunctivitis was induced in actively sensitized guinea pigs, and the scratching behavior was observed upon antigen challenge. The scratching behavior to the eye of guinea pigs was significantly inhibited by **ketotifen ophthalmic** solution, although solns. of disodium cromoglycate and tranilast failed to affect it. These results support the anti-pruritic efficacy of ketotifen in humans, which is mainly due to its histamine H1 receptor antagonistic property.

L2 ANSWER 71 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 41
AN 2001:8432 BIOSIS
DN PREV200100008432
TI A forced choice comfort study of olopatadine hydrochloride 0.1% versus ketotifen fumarate 0.05%.
AU Artal, Maria Natalia [Reprint author]; Luna, Jose Domingo [Reprint author]; Discepola, Marino
CS Fundacion VER, 5000, Cordoba, Argentina
SO Acta Ophthalmologica Scandinavica, (June, 2000) Vol. 78, No. Supplement 230, pp. 64-65. print.
ISSN: 1395-3907.
DT Article
LA English
ED Entered STN: 21 Dec 2000
Last Updated on STN: 21 Dec 2000
AB Purpose: To compare the ocular comfort of two ophthalmic anti-allergic agents: olopatadine hydrochloride 0.1% and ketotifen fumarate 0.05%. Subjects and Methods: In a double-masked, multi-centered, randomized trial, 80 subjects were asked to make a 'forced choice' based on ocular comfort between one drop of olopatadine hydrochloride 0.1% instilled in one eye and one drop of ketotifen fumarate 0.05% instilled in the contralateral eye. At one site, the incidence of adverse reactions was also reported. Results: All subjects (100%) selected olopatadine as the more comfortable formulation. One site (n=35) reported a 49% incidence of moderate burning and a 49% incidence of mild burning after ketotifen instillation. One subject (2% of population) at this site experienced no ocular discomfort with ketotifen. There were no reports of discomfort associated with olopatadine instillation. Conclusion: Olopatadine is a more comfortable **ophthalmic** preparation than **ketotifen**
.

L2 ANSWER 72 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 42
AN 131:106822 CA

TI Autoclavable pharmaceutical compositions containing a chelating agent
IN Kis, Gyorgy Lajos
PA Novartis A.-G., Switz.; Novartis-Erfindungen Verwaltungsgesellschaft m.b.H.
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9936055	A1	19990722	WO 1999-EP160	19990113
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	EP 938896	A1	19990901	EP 1998-810016	19980115
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	CA 2315767	AA	19990722	CA 1999-2315767	19990113
	AU 9926169	A1	19990802	AU 1999-26169	19990113
	AU 742920	B2	20020117		
	EP 1047406	A1	20001102	EP 1999-906123	19990113
	EP 1047406	B1	20030423		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	EP 1172098	A1	20020116	EP 2001-124282	19990113
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002509101	T2	20020326	JP 2000-539830	19990113
	AT 238036	E	20030515	AT 1999-906123	19990113
	PT 1047406	T	20030829	PT 1999-906123	19990113
	ES 2198127	T3	20040116	ES 1999-906123	19990113
	US 6468548	B1	20021022	US 2000-616151	20000714
	US 2002165254	A1	20021107	US 2001-16361	20011210
	US 6776982	B2	20040817		
PRAI	EP 1998-810016	A	19980115		
	EP 1999-906123	A3	19990113		
	WO 1999-EP160	W	19990113		
	US 2000-616151	A3	20000714		

AB An autoclavable ophthalmic composition comprises an ophthalmic drug stabilized against thermal decomposition during autoclaving by addition of a chelating agent (EDTA, Dequest, Desferal). The chelating agent acts synergistically with preservatives in the composition, thereby reducing the amount of preservative required. Thus, eye drops containing ketotifen H fumarate 0.0345 mg, glycerol 2.550, di-Na edetate 0.05, benzalkonium chloride 0.01, 1N NaOH 0.083 g, and H2O for injection to 100 mL (pH 5.31), when autoclaved at 120° and 1.5 bar for 20 min, still had a ketotifen H fumarate content 98.2% of that before autoclaving and contained no detectable degradation products of ketotifen.

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 73 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 43
AN 131:92506 CA
TI Eye drops containing ketotifen and vitamins
IN Okudaira, Ichiro; Sumida, Kenji
PA Taisho Pharmaceutical Co., Ltd., Japan

SO Jpn. Kokai Tokkyo Koho, 5 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP 11189533	A2	19990713	JP 1997-356858	19971225
PRAI JP 1997-356858		19971225		

AB Eye drops for the treatment of conjunctivitis, especially inflamed conditions comprise ketotifen or its salts and vitamins. An eye drop solution contained ketotifen fumarate 25, vitamin B6 100, dipotassium glycyrrhizinate 300, lidocaine hydrochloride 250 mg, and 100 mL distilled water.

L2 ANSWER 74 OF 90 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
AN 1999-29604 DRUGU T S
TI Aspirin sensitivity: the role for aspirin challenge and desensitization in postmyocardial infarction patients.
AU Schaefer O P; Gore J M
CS Univ.Massachusetts
LO Worcester, Mass., USA
SO Cardiology (91, No. 1, 8-13, 1999) 1 Fig. 3 Tab. 27 Ref.
CODEN: CAGYAO ISSN: 0008-6312
AV Division of Pulmonary, Allergy and Critical Care Medicine, University of Massachusetts Medical Center, 55 Lake Avenue, North Worcester, MA 01655, U.S.A. (e-mail: oren.schaefer@banyan.ummed.edu).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB 2 Cases of possible aspirin (AS) hypersensitivity in patients where AS was indicated for secondary prophylaxis of myocardial infarction (MI) are reported. Sensitivity testing indicated 2 of these patients, including 1 initially administered p.o. ticlopidine (TI) post-MI, were not sensitive to AS and were subsequently treated with p.o. AS. An elderly patient treated with heparin and i.v. nitroglycerin was also started on TI (Ticlid) prophylaxis. Mild airflow obstruction was treated with inhaled fluticasone and albuterol (AL). A positive response to AS challenge was treated with AL, oxymetalazone nasal spray and **ophthalmic** naphazoline/**pheniramine**. AS therapy was administered after successful desensitization.

L2 ANSWER 75 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 44
AN 129:335778 CA
TI Eye drops containing vasoconstrictor and ketotifen
IN Okudaira, Ichiro; Tsunoda, Kenji
PA Taisho Pharmaceutical Co., Ltd., Japan
SO PCT Int. Appl., 11 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9847510	A1	19981029	WO 1998-JP1918	19980424
W: AU, CA, CN, KR, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 11005750	A2	19990112	JP 1998-112392	19980422
AU 9870815	A1	19981113	AU 1998-70815	19980424
PRAI JP 1997-107850		19970424		
WO 1998-JP1918		19980424		

AB Eye drops contain a vasoconstrictor and ketotifen or its salt. The eye drops relieve, in particular, ophthalmic mucosal congestion among various

symptoms of conjunctivitis.
RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 76 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 45
AN 126:242892 CA
TI Ophthalmic pharmaceuticals containing O-carboxyalkyl chitosan
IN Reed, Kenneth W.; Yen, Shau-Fong
PA Ciba-Geigy A.-G., Switz.; Reed, Kenneth W.; Yen, Shau-Fong
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9706782	A1	19970227	WO 1996-EP3477	19960806
	W: AL, AU, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	TW 389694	B	20000511	TW 1995-84113923	19951227
	AU 9667897	A1	19970312	AU 1996-67897	19960806
	EP 844868	A1	19980603	EP 1996-928418	19960806
	EP 844868	B1	20011024		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11510497	T2	19990914	JP 1997-507926	19960806
	AT 207343	E	20011115	AT 1996-928418	19960806
	PT 844868	T	20020328	PT 1996-928418	19960806
	ES 2166905	T3	20020501	ES 1996-928418	19960806
PRAI	US 1995-516420	A	19950817		
	WO 1996-EP3477	W	19960806		

AB Ophthalmic pharmaceuticals containing O-carboxyalkyl chitosan (I) are disclosed. I enhances ocular bioavailability and is especially useful in ophthalmic compns. which must be held at an acidic pH for storage, and which must remain clear when applied to the eye at a physiol. pH of about 7.4. An ophthalmic solution contained glacial acetic acid 5, sodium chloride 6, N,O-carboxymethyl chitosan 40, pilocarpine 20 g, and water 900 mL; pH = 5. The composition performed similarly to Sperasacarpine (containing 4.5 mg/mL HPMC) in miosis profile as a function of time.

L2 ANSWER 77 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 46
AN 126:162281 CA
TI Ophthalmic compositions and methods for stabilizing polymers
IN Tsao, Fu-Pao
PA Ciba-Geigy A.-G., Switz.; Tsao, Fu-Pao
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9700669	A1	19970109	WO 1996-EP2539	19960612
	W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5683993	A	19971104	US 1995-493761	19950622

	CA 2222646	AA	19970109	CA 1996-2222646	19960612
	AU 9663551	A1	19970122	AU 1996-63551	19960612
	AU 715686	B2	20000210		
	EP 833609	A1	19980408	EP 1996-922797	19960612
	EP 833609	B1	20011107		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11510480	T2	19990914	JP 1997-503430	19960612
	AT 208189	E	20011115	AT 1996-922797	19960612
	PT 833609	T	20020429	PT 1996-922797	19960612
	ES 2167581	T3	20020516	ES 1996-922797	19960612
	US 5858996	A	19990112	US 1997-863855	19970527
PRAI	US 1995-493761	A2	19950622		
	WO 1996-EP2539	W	19960612		

AB Ophthalmic compns. and methods for reducing the decomposition rate of polymeric bioadhesives and viscosity enhancers, such as poly(acrylic acids) are described. The compns. include at least 1 strong, stable chelating agent, preferably an organophosphorous compound such as diethylenetriamine pentamethylene phosphonic acid. Thus, a composition was prepared by mixing Noveon AA1 0.625, NaCl 0.6, PEG 400 0.2, Dequest 2060 0.006, and Dextran 70 0.1%, and qs water. The pH of the solution was adjusted to 6.8, and the viscosity of the composition was determined

L2 ANSWER 78 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 47
AN 124:270573 CA
TI Eye drops of ketotifen fumarate
IN Masubuchi, Harumi; Ono, Kazuhiro
PA Showa Pharm Chem Ind, Japan
SO Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 08020538	A2	19960123	JP 1994-153633	19940705
	JP 3055753	B2	20000626		
PRAI	JP 1994-153633		19940705		

AB The eye drops contain ketotifen fumarate (I), water-soluble organic acids and/or their salts, and H2O. The eye drops show improved storage stability. I (0.69 g) and 20 g Na citrate were dissolved in H2O and the solution was adjusted to pH 5.2 then diluted to 1000 mL to give an eye drop. The eye drop was stored at 70° for 6 days to show remaining rate of I 98% and no change in the appearance, while a control containing Me cellulose as a stabilizer became cloudy with remaining rate 94%.

L2 ANSWER 79 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 48
AN 124:185628 CA
TI Stable eye lotions of ketotifen fumarate
IN Takanobu, Kyoshi; Noto, Mitsuru; Oguro, Susumu; Saiki, Yoshinori; Tatsuta, Misa
PA Toa Yakuhin Kk, Japan
SO Jpn. Kokai Tokkyo Koho, 4 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 07324034	A2	19951212	JP 1994-139305	19940530
PRAI	JP 1994-139305		19940530		

AB The eye lotions containing ketotifen fumarate (I) and boric acid and optional chelating agents or chelating agents and amino acids are claimed. The eye

lotions are excellent in stability of I and have less irritating action. I 100, boric acid 1500, and benzalkonium chloride 10 mg were dissolved in H2O and the solution was adjusted to pH 5.2, then diluted to give 100 mL eye lotion. The eye lotion was stored in a brass bottle at 90° for 18 h or in a plastic bottle at 60° for 1 mo to show the remaining rate of I 100.4 or 102.6%, resp., vs. 94.8 or 97.4%, resp., for a control lotion containing 2500 mg glycerin instead of boric acid.

L2 ANSWER 80 OF 90 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
AN 1993-18695 DRUGU P
TI Effect of Naphcon-A on Histamine Skin Test Reactivity.
AU Lantner R; Espiritu B; Tobin M
LO Maywood, Illinois, United States
SO J.Allergy Clin.Immunol. (91, No. 1, Pt. 2, 364, 1993)
CODEN: JACIBY ISSN: 0090-7421
AV No Reprint Address).
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB The effect of Naphcon-A (NA) **ophthalmic** solution (naphazoline HCl, and **pheniramine** maleate; Alcon) was studied on histamine (H) skin test reactivity in 15 subjects. It is concluded that NA does not inhibit H skin test reactivity and should not interfere with allergy skin testing during normal use. (congress abstract).

L2 ANSWER 81 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 49
AN 115:214865 CA
TI Ophthalmic compositions containing antiallergics and antihistamines
IN York, Billie M.; Robertson, Stella M.
PA Alcon Laboratories, Inc., USA
SO Eur. Pat. Appl., 6 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 433766	A1	19910626	EP 1990-123298	19901205
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AU 9067740	A1	19910620	AU 1990-67740	19901204
	AU 636685	B2	19930506		
	CA 2031593	AA	19910619	CA 1990-2031593	19901205
	ZA 9009941	A	19911030	ZA 1990-9941	19901211
	JP 04009339	A2	19920114	JP 1990-410621	19901214
	US 5192780	A	19930309	US 1991-734728	19910723
PRAI	US 1989-452189		19891218		
	US 1990-616049		19901120		

AB A pharmaceutical composition for the prevention and treatment of ophthalmic allergic response comprises an antiallergy compound 0.01-4.0 and an antihistamine 0.0103.0%. An **ophthalmic** composition contained **pheniramine** maleate 0.297, lodoxamide tromethamine 0.178, Na citrate-2H2O 0.0415, citric acid-2H2O 0.01755, mannitol 4.4, tyloxapol 0.025, Na2EDTA 0.01, benzalkonium chloride 0.007, HPMC 0.38, NaOH or HCl to adjust pH to 5, and water to 100% weight/volume

L2 ANSWER 82 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1991:243792 BIOSIS
DN PREV199140117957; BR40:117957
TI EFFECTS OF PEMIROLAST POTASSIUM A NOVEL ANTIALLERGIC AGENT ON EXPERIMENTAL OCULAR ALLERGIC REACTION.
AU HIKIDA M [Reprint author]; MIBU H; SAWA K; KUROSE T; DOURA Y; YAMAGUCHI H; HAYASHI M

CS CENT RES LAB, SANTEN PHARMACEUTICAL CO LTD, OSAKA, JAPAN
SO Investigative Ophthalmology and Visual Science, (1991) Vol. 32, No. 4, pp. 683.
Meeting Info.: ANNUAL SPRING MEETING OF THE ASSOCIATION FOR RESEARCH IN VISION AND OPTHALMOLOGY, SARASOTA, FLORIDA, USA, APRIL 28-MAY 3, 1991.
INVEST OPHTHALMOL VISUAL SCI.
CODEN: IOVSDA. ISSN: 0146-0404.
DT Conference; (Meeting)
FS BR
LA ENGLISH
ED Entered STN: 21 May 1991
Last Updated on STN: 16 Jul 1991

L2 ANSWER 83 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1991:413282 BIOSIS
DN PREV199192080247; BA92:80247
TI MEDICAL MANAGEMENT OF VERNAL CONJUNCTIVITIS CRITICAL EVALUATION.
AU DE FRANCO N [Reprint author]; BATTISTINI P; MARIOTTI C; LUCIANI G
CS CLINICA OCULISTICA UNIVERSITA ANCONA, ITALY
SO Bollettino di Oculistica, (1991) Vol. 70, No. 2, pp. 309-316.
ISSN: 0006-677X.
DT Article
FS BA
LA ITALIAN
ED Entered STN: 11 Sep 1991
Last Updated on STN: 13 Nov 1991
AB The sole use of disodium cromoglycate- (DSCG-) or corticosteroid-based products in presence of vernal conjucntivitis does not give a prompt relief to the patient; the simultaneous administration of decongestants and antihistamines produces a rapid amelioration of symptoms and an optimal compliance. An open, controlled, clinical trial was carried out on thirty-eight patients (average age 32.8 yr), randomly divided into two groups of 19 subjects each, suffering from vernal conjunctivitis. The trial was aimed at evaluating the therapeutic role of a preservative-free association of 0.05% tetrahydrozoline and 0.3% pheniramine maleate (Tetramil Monodose eyedrops) compared with a 4% DSCG and 0.2% chlorphenamine association. The dose was for Tetramil 2 drops three times a day, for the other preparation 2 drops four time a day. The duration of treatment was 14 days. On the first day, after the basal recording of parameters (hyperemia, itching, photophobia, lacrimation, foreign body sensation) 2 drops of each preparation were administered and parameters recorded after 5, 10, 20 and 30 minutes. On the 7th and 14th days of treatment, parameters were recorded in the morning prior to the first administration. The pharmacodynamic test showed that Tetramil-treated group had a more favourable response to treatment in comparison with the other group, particularly on hyperemia (after 5': 45% reduction with Tetramil and -3% with the comparison; after 30': -87% and -41% respectively) and on itching sensation (after 30': Tetramil -77.8%, comparison -54.6%). The deferred tests showed that both preparations have good efficacy, but some symptoms (hyperemia, itching, foreign body sensation) showed a better amelioration with Tetramil.

L2 ANSWER 84 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1989:476237 BIOSIS
DN PREV198988111997; BA88:111997
TI TOPICAL KETOTIFEN SUPPRESSED OCULAR PROVOCATION FOR JAPANESE CEDAR POLLINOSIS.
AU SAKUMA Y [Reprint author]; MITA H
CS DEP OPHTHALMOL, NATL SAGAMIHARA HOSP, 18-1, SAKURADAI, SAGAMIHARA, 228, JPN
SO Rinsho Ganka, (1989) Vol. 43, No. 8, pp. 1251-1254.
CODEN: RIGAA3. ISSN: 0370-5579.

DT Article
FS BA
LA JAPANESE
ED Entered STN: 17 Oct 1989
Last Updated on STN: 23 Oct 1989
AB We evaluated the value of 0.05% **ketotifen** (HC) **ophthalmic** solution in the inhibition of release of histamine in the tear fluid after eye provocation with antigen for Japanese cedar pollinosis. A series of 11 patients were tested during the off-season. HC was instilled in the right eye, while the left eye was given placebo eyedrops. Five minutes later, both eyes were instilled with cedar antigen solution at 1:20 w/v. Levels of histamine in collected tear sample before, 5 and 10 minutes after provocation, were determined by radioimmunoassay, we observed significant inhibitory effects on histamine release in eyes treated with HC, $p < 0.01$ each at 5 and 10 minutes. The actual rate of inhibition of release of histamine amounted to 67.5% at 5 minutes and 67.2% at 10 minutes. The findings seem to suggest the possible clinical usefulness of HC for Japanese cedar pollinosis.

L2 ANSWER 85 OF 90 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
AN 1988-32662 DRUGU A G
TI Analysis of Some Dosage Forms Containing Pyridine Derivatives Using a Cyclodextrin Bonded Stationary Phase in HPLC.
AU Rabbat N El; Omar N; Gezawi S El; Perrin J H
LO Assiut, Egypt; Gainesville, Florida, United States
SO J.Pharm.Biomed.Anal. (6, No. 4, 393-98, 1988) 2 Fig. 4 Tab. 4 Ref.
CODEN: JPBADA ISSN: 0022-3573
AV Department of Pharmacy, University of Assiut, Assiut, Egypt.
LA English
DT Journal
FA AB; LA; CT; MPC
FS Literature
AB An HPLC method using a silica bound to beta cyclodextrin (Cyclobond I) as column packing is described for the determination of pyridine containing drugs. A mobile phase of methanol/phosphate buffer (pH 7) was used with photometric detection. This method was successfully applied to the analysis of tropicamide in Mydrialcyl (Alcon) **ophthalmic** solution, **pheniramine** maleate and phenylephrine HCl in Dristan (Whitehall) nasal spray, pheniramine maleate in Verstat (Saron, also contains nicotinic acid) capsules, triprolidine HCl and pseudoephedrine HCl in Actifed (Wellcome) tablets and phenypropanolamine HCl, pheniramine maleate and pyrilamine maleate in Triaminic (Dorsey) tablets.

L2 ANSWER 86 OF 90 CA COPYRIGHT 2004 ACS on STN DUPLICATE 50
AN 109:11744 CA
TI **Ophthalmic** solutions containing **ketotifen** fumarate
IN Kurasawa, Tokio; Ueda, Shogo
PA Sankyo Co., Ltd., Japan
SO Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 62277323	A2	19871202	JP 1986-187991	19860811
PRAI	JP 1986-34476		19860219		

AB An **ophthalmic** solution comprises **ketotifen** fumarate and a polyhydric alc. as an isotonic agent. Ketotifen fumarate 1.0, benzalkonium chloride 0.1, and mannitol 50 g were dissolved in 800 mL distilled water; to the solution was added NaOH to adjust pH to 5.0; and the volume was adjusted to 1000 mL with distilled water. After storage of the solution for 16 h at 100°, 86% ketotifen fumarate of the original content remained intact, compared to 39% for control solution containing NaCl

g instead of mannitol 50 g.

L2 ANSWER 87 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1986:273235 BIOSIS
DN PREV198631018155; BR31:18155
TI EVALUATION OF AN ANTIHISTAMINE-DECONGESTANT FOR RAGWEED ALLERGIC CONJUNCTIVITIS WITH GRADED PROVOCATIVE TESTING.
AU DONNENFELD E D [Reprint author]; NAIDOFF M A; SACCAR C L; MANSMANN H C JR; PERRY H D
CS NORTH SHORE UNIV HOSP
SO Investigative Ophthalmology and Visual Science, (1986) Vol. 27, No. 3 SUPPL, pp. 247.
Meeting Info.: ANNUAL SPRING MEETING OF THE ASSOCIATION FOR RESEARCH IN VISION AND OPHTHALMOLOGY INCORPORATED, SARASOTA, FLA., USA, APR. 28-MAY 2, 1986. INVEST OPHTHALMOL VISUAL SCI.
CODEN: IOVSDA. ISSN: 0146-0404.
DT Conference; (Meeting)
FS BR
LA ENGLISH
ED Entered STN: 28 Jun 1986
Last Updated on STN: 28 Jun 1986

L2 ANSWER 88 OF 90 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
AN 1985-22153 DRUGU T
TI Evaluation of an Antihistamine-Decongestant in the Treatment of Ragweed Mediated Ocular Allergy.
AU Saccar C L; Mansmann H C Jr; Martynec D; Naidoff M A; Elvey S M; Donnenfeld E
LO Philadelphia, Pennsylvania, United States
SO Ann.Allergy (54, No. 4, 346, 1985)
CODEN: ANAEA3 ISSN: 0003-4738
AV No Reprint Address.
LA English
DT Journal
FA LA; CT
FS Literature
AB Muro's Opcon-A (MOA), an antihistamine decongestant **ophthalmic** (naphazoline + **pheniramine** maleate) was evaluated in comparison to Muro's Opcon (MO), a decongestant (naphazoline) and placebo (P) for the treatment (TX) of ragweed (R) mediated ocular allergy. 21 Patients (19-44 yr) with allergic conjunctivitis and R IgE-mediated hypersensitivity were studied in double-blind, randomized, 3-way crossover schedule of 8 days/TX. Efficacy was assessed on the basis of physician's rating of signs and symptoms patient's rating of product acceptance response to histamine and global assessment. Results are tabulated. MOA demonstrated best improvement. (congress abstract).

L2 ANSWER 89 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 51
AN 1982:313068 BIOSIS
DN PREV198274085548; BA74:85548
TI THERAPEUTIC EFFECTS OF A NEW ANTI ALLERGIC OPHTHALMIC PREPARATION.
AU MIKUNI I [Reprint author]; FUJIWARA T; TOGAWA K; MOCHIDA H; ARAI Y; KUBOTA A; MIZUSHIMA N
CS DEP OPHTHALMOLOGY, SCH MED, TOKAI UNIV, BOHSEIDAI, ISEHARA, KANAGAWA 259-11, JPN
SO Tokai Journal of Experimental and Clinical Medicine, (1982) Vol. 7, No. 2, pp. 279-294.
CODEN: TJEMDR. ISSN: 0385-0005.
DT Article
FS BA
LA ENGLISH
AB A 0.1% **Ketotifen ophthalmic** preparation was evaluated

in 11 [human] cases of conjunctivitis due to Japanese cedar pollinosis (3 cases also associated with vernal catarrh). Results were obtained concerning the safety and the therapeutic efficacy of the preparation. In the computation of the overall effects of the preparation, a marked therapeutic effect was noted in 3 of 11 cases studied while 1 case remained unaffected. The overall effective rate was 91%. The time required for the preparation to take effect was ≤ 3 days in 7 cases (70.0%) and 10 in which therapeutic effects were noted. In observations of the adverse effects of the preparation, transient irritation at the site of application was noted in 7 cases. No other serious side effects were recorded. The preparation is apparently an effective therapeutic agent for conjunctivitis caused by pollinosis.

L2 ANSWER 90 OF 90 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1983:242701 BIOSIS
DN PREV198376000193; BA76:193
TI TREATMENT OF ALLERGIC CONJUNCTIVITIS WITH OCULAR DECONGESTANTS.
AU SMITH J P [Reprint author]; LANIER B Q; TREMBLAY N; WARD R L; DEFALLER J M
CS NEW PRODUCT RES-MED DEP, ALCON LABS INC, 6201 S FREEWAY, PO BOX 1959, FORT WORTH, TEX 76101, USA
SO Current Eye Research, Vol. 2, No. 2, pp. 141-147. 1982-1983.
CODEN: CEYRDM. ISSN: 0271-3683.
DT Article
FS BA
LA ENGLISH
AB Three commercially available ocular decongestant products which contain varying concentrations of a vasoconstrictor (naphazoline hydrochloride) and an antihistamine (antazoline phosphate or pheniramine maleate) were tested for comfort and therapeutic efficacy. Three separate studies were performed: a comfort comparison, a vasoconstrictive efficacy test using an in vivo model of allergic conjunctivitis induced by compound 48/80 [product of 4-', methoxy-N-methylbenzene methyl-anamine and formaldehyde], and a clinical trial of therapeutic efficacy in patients with allergic/hay fever conjunctivitis. The 3 preparations varied greatly in patient comfort and acceptability but were not different in their ability to ameliorate the itching, tearing, redness, edema and discomfort that occur in human allergic conjunctivitis.

=> s ophthalmic (5a) (antazoline or azelastine)
L3 83 OPHTHALMIC (5A) (ANTAZOLINE OR AZELASTINE)

=> dup remove L3
PROCESSING COMPLETED FOR L3
L4 42 DUP REMOVE L3 (41 DUPLICATES REMOVED)

=> d L4 1-42 bib, ab

L4 ANSWER 1 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2004:209173 BIOSIS
DN PREV200400210047
TI Patient evaluation of **azelastine ophthalmic** solution in allergic conjunctivitis.
AU Siegel, C. J. [Reprint Author]; Kanter, L. J.
CS University of Missouri, Kansas City, MO, USA
SO Journal of Allergy and Clinical Immunology, (February 2004) Vol. 113, No. 2 Supplement, pp. S217. print.
Meeting Info.: 60th Annual Meeting of the American Academy of Allergy, Asthma and Immunology (AAAAI). San Francisco, CA, USA. March 19-23, 2004. American Academy of Allergy, Asthma and Immunology.
CODEN: JACIBY. ISSN: 0091-6749.
DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 14 Apr 2004
Last Updated on STN: 14 Apr 2004

L4 ANSWER 2 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 1
AN 140:31454 CA
TI Pharmaceutical composition comprising azelastine and steroid
IN Lulla, Amar; Malhotra, Geena
PA Cipla Limited, India
SO Brit. UK Pat. Appl., 12 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI GB 2389530	A1	20031217	GB 2002-13739	20020614
WO 2003105856	A1	20031224	WO 2003-GB2557	20030613

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI GB 2002-13739 A 20020614
AB A pharmaceutical composition comprises azelastine or a salt thereof, and a steroid, the composition being in a form suitable for nasal or ocular administration. Preferred steroids include beclomethasone, mometasone, fluticasone, budesonide and cyclosenide and preferred formulations include aerosols, ointments, eye drops, nasal drops or sprays, inhalation solns. or insufflation powders. Also provided is a method of treating irritation or disorders of the nose and eye comprising applying directly to nasal tissues or to the conjunctival sac of the eyes, a medicament which contains a member selected from the group consisting of azelastine and its pharmaceutically acceptable salts, in combination with a steroid.
RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 2
AN 139:239955 CA
TI Topical azelastine in perennial allergic conjunctivitis
AU Canonica, G. W.; Ciprandi, G.; Petzold, U.; Kolb, C.; Ellers-Lenz, B.; Hermann, R.
CS Allergy and Respiratory Diseases, Department of Internal Medicine, University of Genoa, Genoa, Italy
SO Current Medical Research and Opinion (2003), 19(4), 321-329
CODEN: CMROCX; ISSN: 0300-7995
PB LibraPharm Ltd.
DT Journal
LA English
AB Objective: Azelastine is a selective H1-receptor antagonist that inhibits histamine release and interferes with activation of several other mediators of allergic inflammation. Together with demonstrated efficacy in seasonal allergic conjunctivitis, azelastine indicated a therapeutic potential for perennial allergic conjunctivitis (PAC). The present study aimed to evaluate azelastine eye drops in patients with PAC compared to placebo. Research design and methods: A multinational trial in 22 centers randomized 139 patients to twice-daily treatment for 6 wk with masked

0.05% azelastine eye drops, matching masked placebo, or open-label levocabastine. Randomization required a sum itching and conjunctival redness score of at least 3 (0-6 scale) after 1 wk of placebo. The change in sum score was evaluated during treatment. Results: Azelastine significantly improved itching and conjunctival redness compared to placebo ($p < 0.001$) with global tolerability that was not substantially different from placebo. On day 7, the mean symptoms sum score improved with azelastine by 1.9±1.1 and with levocabastine by 1.5±1.2 compared to placebo (0.6±1.1) from baseline values of 3.7-3.8. The sum scores continued to improve up to day 42. Daily patient logs confirmed the clin. assessed scores. Most frequent adverse events following azelastine were bitter taste and application site reaction. Conclusions: Topical azelastine progressively improved itching and conjunctival redness in PAC patients compared to placebo and was at least as effective as levocabastine. Rapid relief is consistent with H1-receptor antagonist action, while continued improvement up to 6 wk may be consistent with mechanisms involving other mediators of allergic inflammation.

RE.CNT 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 3

AN 141:17150 CA

TI Azelastine Inhibits Secretion of IL-6, TNF-α and IL-8 as well as NF-κB Activation and Intracellular Calcium Ion Levels in Normal Human Mast Cells

AU Kempuraj, Duraisamy; Huang, Man; Kandere-Grzybowska, Kristiana; Basu, Subimal; Boucher, William; Letourneau, Richard; Athanassiou, Achilles; Theoharides, Theoharis C.

CS Department of Pharmacology and Experimental Therapeutics, Tufts University School of Medicine and Tufts-New England Medical Center, Boston, MA, USA

SO International Archives of Allergy and Immunology (2003), 132(3), 231-239
CODEN: IAAIEG; ISSN: 1018-2438

PB S. Karger AG

DT Journal

LA English

AB Background: Mast cells are involved in allergic inflammation by secreting histamine, proteases and several cytokines, including interleukin (IL)-6, tumor necrosis factor-α (TNF-α) and IL-8. Certain histamine-1 receptor antagonists, such as **azelastine** present in the **ophthalmic** solution Optivar, have been reported to inhibit histamine and tryptase secretion, but its effect on inflammatory cytokine release from normal human umbilical cord blood-derived cultured mast cells (hCBMC) are not well known. Methods: We investigated the effect of azelastine on the secretion of IL-6, TNF-α and IL-8 from hCBMC, as well as its possible mechanism of action. hCBMC sensitized with IgE were pretreated for 5 min with azelastine at 0.01, 0.1, 1, 3, 6, 12, 24, or 60 μM of Optivar before stimulation with anti-IgE for 6 h. Optivar vehicle without azelastine was used as control. Cytokines were measured by ELISA, intracellular calcium levels by calcium indicators confocal, and nuclear factor-κB (NF-κB) by electromobility shift assay. Results: Stimulation with anti-IgE led to substantial secretion of IL-6, TNF-α and IL-8. Preincubation for 5 min resulted in almost maximal inhibition with 6 μM azelastine for TNF-α (80%), with 24 μM for IL-6 (83%) and 60 μM for IL-8 (99%); the vehicle solution at the same concns. as Optivar had no effect. Stimulation with anti-IgE increased intracellular Ca2+ level and induced NF-κB expression in hCBMC, which was inhibited by 24 μM azelastine. Conclusion: Azelastine inhibited hCBMC secretion of IL-6, TNF-α and IL-8, possibly by inhibiting intracellular Ca2+ ions and NF-κB activation. Azelastine may, therefore, be helpful in treating allergic inflammation.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 4

AN 139:17309 CA
TI Azelastine eye drops in the treatment of perennial allergic conjunctivitis
AU Nazarov, Ozod; Petzold, Ursula; Haasec, Hans; Nguyen, Duc Tung; Ellers-Lenz, Barbara; Hermann, Robert
CS Scientific Center for Allergy of Uzbekistan, Tashkent, Uzbekistan
SO Arzneimittel-Forschung (2003), 53(3), 167-173
CODEN: ARZNAD; ISSN: 0004-4172
PB Editio Cantor Verlag
DT Journal
LA English
AB Azelastine (CAS 58581-89-8) is a selective H1-receptor antagonist that inhibits histamine release and interferes with activation of other mediators of allergic inflammation. The present double-blind study aimed to evaluate azelastine eye drops (Allergodil) in patients with perennial allergic conjunctivitis compared to placebo. A total of 116 patients with an ocular symptoms score for itching and conjunctival redness ≥3 (0-6 scale) were randomized to twice-daily 0.05% azelastine eye drops treatment (n = 58) or placebo. Patients maintained daily logs and were clin. evaluated after 7, 21 and 42 days of treatment. Azelastine significantly improved itching and conjunctival redness vs. placebo ($p < 0.001$). Tolerability was rated good or better by 97% of patients with only bitter taste and application site reaction notable adverse experiences. On Day 7, ocular symptoms score improved by 1.5±0.9 (vs. 0.5±0.8 placebo) with score improvement ≥2 in 55% with azelastine (vs. 14% placebo). Itching and redness further improved at Day 42 (score improvement ≥2 in 95% with azelastine vs. 33% placebo) and completely resolved for 47% azelastine patients (vs. 10% placebo). Daily patient logs confirmed the clin. assessed scores. Topical azelastine progressively improved itching and conjunctival redness in patients with moderate to severe perennial allergic conjunctivitis. Continued improvement with prolonged use is consistent with mechanisms other than H1-receptor blockade, such as possible down regulation of adhesion mol. receptors.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 5
AN 140:122376 CA
TI Azelastine is more potent than olopatadine in inhibiting interleukin-6 and tryptase release from human umbilical cord blood-derived cultured mast cells
AU Kempuraj, Duraisamy; Huang, Man; Kandere, Kristiana; Boucher, William; Letourneau, Richard; Jeudy, Sheila; Fitzgerald, Kim; Spear, Kathleen; Athanasiou, Achilles; Theoharides, Theoharis C.
CS Department of Pharmacology and Experimental Therapeutics, Tufts University School of Medicine and New England Medical Center, Boston, MA, USA
SO Annals of Allergy, Asthma, & Immunology (2002), 88(5), 501-506
CODEN: ALAIF6; ISSN: 1081-1206
PB American College of Allergy, Asthma, & Immunology
DT Journal
LA English
AB Background: Mast cells are involved in early- and late-phase reactions by releasing vasoactive mols., proteases, and cytokines. Certain histamine-1 receptor antagonists and other antiallergic drugs seem to inhibit the release of mediators from rat and human mast cells. Objective: Azelastine and olopatadine are antiallergic agents present in the **ophthalmic** solns. **azelastine** hydrochloride (Optivar, Asta Medica/Muro Pharmaceuticals, Tewksbury, MA), and olopatadine hydrochloride (Patanol, Alcon Labs., Fort Worth, TX), resp. The authors investigated the effect of these drugs on interleukin-6 (IL-6), tryptase, and histamine release from cultured human mast cells (CHMCs). Methods: CHMCs were grown from human umbilical cord blood-derived CD34+ cells in the presence of stem cell factor and IL-6 for 14 to 16 wk. Sensitized CHMCs were pretreated with various concns. of azelastine or olopatadine for 5 min. CHMCs were

then challenged with anti-IgE, and the released mediators were quantitated. Results: The greatest inhibition of mediator release was seen with 24 μM azelastine; this level of inhibition was matched with the use of 133 μM olopatadine. At this concentration, these drugs inhibited IL-6 release by 83% and 74%, tryptase release by 55% and 79%, and histamine release by 41% and 45%, resp. Activated CHMCs were characterized by numerous filopodia that were inhibited by both drugs as shown by electron microscopy. Conclusions: These results indicate that azelastine and olopatadine can inhibit CHMCs activation and release of IL-6, tryptase, and histamine. On an equimolar basis, azelastine was a more potent inhibitor than olopatadine.

RE.CNT 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2002:301932 BIOSIS
DN PREV200200301932
TI Azelastine inhibits interleukin-6 (IL-6), IL-8 production by reducing intracellular calcium ion levels in human umbilical cord blood-derived cultured mast cells.
AU Kempuraj, D. [Reprint author]; Huang, M. [Reprint author]; Boucher, W. [Reprint author]; Letourneau, R. [Reprint author]; Athanasiou, A.; Theoharides, T. C. [Reprint author]
CS Tufts University School of Medicine, Boston, MA, USA
SO Journal of Allergy and Clinical Immunology, (January, 2002) Vol. 109, No. 1 Supplement, pp. S324. print.
Meeting Info.: 58th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. New York, NY, USA. March 01-06, 2002. American Academy of Allergy, Asthma, and Immunology.
CODEN: JACIBY. ISSN: 0091-6749.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 22 May 2002
Last Updated on STN: 22 May 2002

L4 ANSWER 8 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2002:289890 BIOSIS
DN PREV200200289890
TI Efficacy and safety of azelastine in allergic conjunctivitis in children.
AU Petzold, Ulla [Reprint author]; Blochin, Bm; Zimmerman, T.; Sabbah, A.; Karafilidis, John; LaVallee, Nicole; Hanrahan, John Patrick
CS Viatris Pharmaceutical/ASTA Medical, Frankfurt, Germany
SO Journal of Allergy and Clinical Immunology, (January, 2002) Vol. 109, No. 1 Supplement, pp. S162. print.
Meeting Info.: 58th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. New York, NY, USA. March 01-06, 2002. American Academy of Allergy Asthma and Immunology.
CODEN: JACIBY. ISSN: 0091-6749.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 15 May 2002
Last Updated on STN: 15 May 2002

L4 ANSWER 9 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 6
AN 137:257373 CA
TI Azelastine's inhibition of histamine and tryptase release from human umbilical cord blood-derived cultured mast cells as well as rat skin mast cell-induced vascular permeability: comparison with olopatadine
AU Lytinas, Michael; Kempuraj, Duraisamy; Huang, Man; Kandere, Kristiana; Boucher, William; Letourneau, Richard; Jeudy, Sheila; Fitzgerald, Kim;

Spear, Kathleen; Athanasiou, Achilles; Theoharides, Theoharis C.
CS Departments of Pharmacology and Experimental Therapeutics, Tufts University School of Medicine and New England Medical Center, Boston, MA, 02111, USA
SO Allergy and Asthma Proceedings (2002), 23(1), 45-51
CODEN: AAPRFV; ISSN: 1088-5412
PB OceanSide Publications, Inc.
DT Journal
LA English
AB Mast cells are involved in early and late-phase reactions by releasing vasoactive mols., proteases, and cytokines. Azelastine and olopatadine are histamine 1 receptor (H-1R) antagonists with antiallergic effects present in the ophthalmic solns. Optivar and Patanol, resp. Because it is difficult to obtain animal or human conjunctival tissue, the authors 1st investigated the effect of these compds. on histamine and tryptase release from cultured human mast cells (CHMCs) grown out of human umbilical cord blood-derived CD34+ cells. Sensitized CHMCs were pretreated with various concns. of azelastine or olopatadine for 5 min. Then, CHMCs were challenged with anti-IgE (IgE) and the released mediators were quantitated. The greatest inhibition of mediator release was seen when CHMCs were pretreated with 24 μM of azelastine or 133 μM of olopatadine (2% dilution of **azelastine** or 5% olopatadine original **ophthalmic** solns., resp.). The authors then studied the drug concns. that gave optimal results on skin vasodilation induced by the mast cell secretagogue compound 48/80. An intradermal injection of 48/80 in rats, to which Evan's blue had been administered via the tail vein, induced substantial dye extravasation. Pretreatment of the injection site for 5 min with either 24 μM of azelastine or 133 μM of olopatadine completely prevented extravasation; this effect was quantitated also by fluorometric assessment of Evan's blue extracted in formamide. Evaluation of skin mast cells from injected sites showed that mast cell degranulation was inhibited greatly. These results indicate that on an equimolar basis, azelastine was a more potent inhibitor than olopatadine of both CHMC and rat skin mast cells activation.
RE.CNT 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 7
AN 136:31450 CA
TI Evaluation of the efficacy of olopatadine hydrochloride 0.1% **ophthalmic** solution and **azelastine** hydrochloride 0.05% **ophthalmic** solution in the conjunctival allergen challenge model
AU Spangler, Dennis L.; Bensch, George; Berdy, Gregg J.
CS Atlanta Allergy and Asthma Clinic, Atlanta, GA, USA
SO Clinical Therapeutics (2001), 23(8), 1272-1280
CODEN: CLTHDG; ISSN: 0149-2918
PB Excerpta Medica, Inc.
DT Journal
LA English
AB Background: Olopatadine hydrochloride 0.1% **ophthalmic** solution and **azelastine** hydrochloride 0.05% **ophthalmic** solution are 2 topical antiallergic agents indicated for the treatment of itching of the eye associated with allergic conjunctivitis. Olopatadine has recently received US Food and Drug Administration (FDA) approval for an expanded indication for the treatment of signs and symptoms of allergic conjunctivitis, including itching, tearing, eyelid swelling, redness, and chemosis. Objective: The purpose of this study was to compare the efficacy of olopatadine hydrochloride vs. azelastine hydrochloride and placebo (artificial tears) in the conjunctival allergen challenge (CAC) model. Methods: This was a prospective, randomized, double-masked, contralaterally controlled, multicenter, allergen-challenge study. Itching was chosen as the primary efficacy variable since it is the only FDA-approved indication these 2 agents have in common. Subjects with a history of allergic conjunctivitis who responded to the CAC at screening

visits 1 and 2 were randomized to 1 of 3 treatment groups: olopatadine in 1 eye and azelastine in the other eye; olopatadine in 1 eye and placebo in the other eye; or azelastine in 1 eye and placebo in the other eye. At the assessment visit (visit 3), subjects received masked study medication according to the randomization scheme. After 5 min, subjects were bilaterally challenged with the allergen concentration that had elicited a pos. conjunctival allergic response at visits 1 and 2. Immediately after challenge, subjects gave itching assessments (scale, 0 = no itching to 4 = severe itching) every 30 s for a total period of 20 min. Mean itching scores for all eyes were compared by treatment. Mean itching scores at each time point were compared between treatments using 2 sample t tests. Results: Of the 180 subjects screened, 111 responded to the CAC at visits 1 and 2 and completed the study; 65% (72/111) of patients were female, 87% (97/111) were white, and 49% (54/111) had brown irides. The mean age was .apprx.40 yr. Seventy-three eyes were treated with olopatadine, 75 with azelastine, and 74 with placebo. A single dose of 1 of the 3 study medications per eye was well tolerated by all subjects. Both treatments were significantly more effective than placebo at reducing itching postchallenge. Olopatadine was significantly more effective than azelastine in reducing itching at 3.5 min through 20 min postchallenge (average mean unit difference of -0.31; $P < 0.05$) in the CAC model. Conclusion: In this population, olopatadine was significantly more effective than azelastine in the management of itching associated with allergic conjunctivitis in the CAC model.

RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 42 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
AN 2001-27641 DRUGU T S
TI Variability of drop comfort and its importance as a criterion in the selection of topical therapy for ocular allergy.
AU Granet D B; D Arienzo P A
CS Catholic-Med.Cent.
LO Brooklyn, N.Y., USA
SO J.Allergy Clin.Immunol. (107, No. 2, Suppl., S215, 2001)
CODEN: JACIBY ISSN: 0090-7421
AV UCSD Abraham Ratner Children's Eye Center, La Jolla, CA, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB 92 Patients with ocular allergy were entered into a randomized, double-masked study and were treated with Patanol (olopatadine HCl) (Group A) or Optivar (**azelastine** HCl) (Group B) topical **ophthalmic** solutions. Patanol was determined to be more comfortable than Optivar in this study. The results emphasize the variability of drop comfort and its importance as a criterion for therapy selection. (conference abstract: American Academy of Allergy, Asthma, and Immunology 57th Annual Meeting, New Orleans, Louisiana, USA, 2001).

L4 ANSWER 12 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2001:42980 BIOSIS
DN PREV200100042980
TI Evaluation of the onset and duration of effect of Azelastine Eye Drops (0.05%) versus placebo in patients with allergic conjunctivitis using an allergen challenge model.
AU Friedlaender, Mitchell H. [Reprint author]; Harris, Judith; LaVallee, Nicole; Russell, Heidy; Shilstone, Jonathan
CS Scripps Clinic, 10666 North Torrey Pines Road, La Jolla, CA, 92037, USA
mfried@scrippsclinic.com
SO Ophthalmology, (December, 2000) Vol. 107, No. 12, pp. 2152-2157. print.
CODEN: OPHTDG. ISSN: 0161-6420.
DT Article

LA English
ED Entered STN: 17 Jan 2001
Last Updated on STN: 12 Feb 2002
AB Objective: The trial evaluated the effectiveness of the investigational antihistaminic and antiallergic compound Azelastine Eye Drops (AZE) in the treatment of allergic conjunctivitis using an allergen challenge model. Design: Randomized, double-blind, placebo-controlled, paired-eye study. Participants: Adults with a history of allergic conjunctivitis (gtoreq2 years) who were asymptomatic throughout the trial, had a positive skin test (cat dander, grass, or ragweed pollen within the last year), and had a positive conjunctival reaction (score 2+ or more for itching and redness in both eyes on a 0-4 scale) during two separate conjunctival provocation tests (CPT) before randomization. Methods: Eighty patients underwent a 2-week screening period (visits 1 and 2) that included a CPT during visit 1 to establish the allergen threshold dose and a second confirmatory CPT performed at visit 2. Eye symptom assessments for itching (evaluated by patient) and conjunctival redness (evaluated by physician) were performed 5 and 10 minutes after CPT using a 5-point scale (from 0 = none to 4+ = severe). Qualified patients were randomized to receive one drop of AZE (0.015 mg of azelastine hydrochloride) in one eye and one drop of placebo in the other eye 20 minutes before CPT at visit 3 (onset) and 8 or 10 hours before CPT at visit 4 (duration). Main Outcome Measures: Individual severity scores for itching (evaluated by patient) and conjunctival redness (evaluated by physician) for each eye at 3, 5, and 10 minutes after CPT at visits 3 and 4 using a 5-point scale (0 = none to 4+ = very severe). Results: Each of the 80 randomized patients completed the trial. Mean itching and conjunctival redness scores at visit 3 (onset) were significantly lower (P < 0.001) in the AZE-treated eyes than in the placebo-treated eyes. At visit 4 (duration), mean itching and conjunctival redness scores (P ltoreq 0.003) for the 8-hour group and mean itching scores (P ltoreq 0.001) for the 10-hour group were significantly lower in the AZE-treated eyes than in the placebo-treated eyes. Significant differences in mean tearing and chemosis severity scores were also seen at visit 3 (onset) and visit 4 (duration) in the AZE-treated eyes when compared with the placebo-treated eyes. Treatment with AZE was well tolerated. Conclusions: Therapy of experimentally induced allergic conjunctivitis with AZE was highly effective, with an onset of action seen within 3 minutes and a duration of effect of at least 8 to 10 hours.

L4 ANSWER 13 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 2000:259603 BIOSIS
DN PREV200000259603
TI Five years retrospective study of the clinical characteristics and therapy in vernal conjunctivitis.
AU Ahuatl, S. [Reprint author]; Baca, O. [Reprint author]; Velasco, R. [Reprint author]; Pernia, A. [Reprint author]
CS Department of Cornea, Fundacion Hospital Nuestra Senora de la Luz, IAP, Mexico City, Mexico
SO IOVS, (March 15, 2000) Vol. 41, No. 4, pp. S366. print.
Meeting Info.: Annual Meeting of the Association in Vision and Opthalmology. Fort Lauderlade, Florida, USA. April 30-May 05, 2000. Association for Research in Vision and Ophthalmology.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 21 Jun 2000
Last Updated on STN: 5 Jan 2002

L4 ANSWER 14 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 8
AN 135:117158 CA
TI Comparison of Azelastine eye drops with levocabastin eye drops in the treatment of seasonal allergic conjunctivitis
AU Giede, C.; Metzenauer, P.; Petzold, U.; Ellers-Lenz, B.

CS Hanau, D-63450, Germany
SO Current Medical Research and Opinion (2000), 16(3), 153-163
CODEN: CMROCX; ISSN: 0300-7995
PB LibraPharm Ltd.
DT Journal
LA English
AB A randomized, multicenter parallel group study was undertaken to compare the efficacy and safety of 0.05% azelastine eye drops (101 patients) in an open manner with 0.05% levocabastine eye drops (103 patients) and in a double-blind manner with placebo (103 patients) during a 14-day treatment period involving patients with seasonal allergic conjunctivitis. The three main eye symptoms, scored on a four-point scale, were itching, lacrimation and conjunctival redness; the primary efficacy variable was the responder rate on day 3. Responders were patients whose sum score of the three main eye symptoms decreased by at least three points from a baseline score of at least six points. In addition to these main symptoms, five other symptoms were recorded on days 0, 3, 7 and 14, and patients kept daily diaries of the three main eye symptoms and swollen eyelids. The responder rate after 3 days of treatment was 69% in patients treated with azelastine, 59% in patients treated with levocabastine and 51% in the placebo group. Only the difference in responder rates between azelastine and placebo eye drops was statistically significant ($p = 0.02$). The improvements in other ocular symptoms and entries in the patients' diaries closely reflected the changes reported by the investigators. No serious adverse events occurred throughout the study. Nine patients (three in the azelastine, five in the levocabastine and one in the placebo group) terminated the study prematurely due to poor tolerability. Adverse drug reactions, mainly a mild, transient irritation and a bitter or unpleasant taste, were reported in 37% of patients receiving azelastine eye drops, 31% of patients receiving levocabastine and 9% of placebo patients. Overall tolerability was assessed as very good or good in 86% of azelastine- and levocabastine-treated patients, and in 95% of the patients receiving placebo. The results of this study indicate that azelastine possesses a tolerability profile at least comparable to that of levocabastine eye drops, but addnl. appears to have a slightly quicker onset of effect, and confirm the therapeutic potential of azelastine eye drops in the treatment of allergic conjunctivitis.
RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1999:270200 BIOSIS
DN PREV199900270200
TI Double-blind comparative and randomized security trial, for ocular tolerance and effectiveness of chlorhydrate of azelastine solution at 0.1% against lodoxamide-trometamine suspension at 0.1% in the treatment of the allergic conjunctivitis.
AU Alcivar-Viteri, R. [Reprint author]; Hernandez-Lopez, A. [Reprint author]; Lopez-Chavez, E. [Reprint author]; Garzon, M. [Reprint author]; Graue-Wiechers, E. [Reprint author]; Espinoza-Velasco, A. [Reprint author]
CS Instituto de Oftalmologia, Universidad Nacional Autonoma de Mexico, Mexico, DF, Mexico
SO IOVS, (March 15, 1999) Vol. 40, No. 4, pp. S914. print.
Meeting Info.: Annual Meeting of the Association for Research in Vision and Ophthalmology. Fort Lauderdale, Florida, USA. May 9-14, 1999. Association for Research in Vision and Opthalmology.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 15 Jul 1999
Last Updated on STN: 15 Jul 1999

L4 ANSWER 16 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 9
AN 130:320813 CA
TI Azelastine eye drops reduce conjunctival hyperresponsiveness to hyperosmolar glucose challenge in children with asymptomatic mite conjunctivitis
AU Ciprandi, G.; Catrullo, A.; Tosca, M.; Cerqueti, P.; Mondino, C.; Passalacqua, G.; Canonica, G. W.
CS Allergy and Clinical Immunology Service, Department of Internal Medicine, Genoa University, Italy
SO Journal of Investigational Allergology & Clinical Immunology (1999), 9(1), 35-38
CODEN: JIAIEF; ISSN: 1018-9068
PB Prous Science, S.A.
DT Journal
LA English
AB Mite allergy is characterized by a continuous allergen exposure. Persistent inflammation is therefore always detectable, and during symptomless periods as well. It has been reported that mite allergic patients also present a nonspecific hyperreactivity to different stimuli, including hyperosmolar solution Since azelastine was previously demonstrated to be able to reduce allergic inflammation, the aim of the study was to investigate the effects of the drug on nonspecific conjunctival hyperreactivity in mite-allergic patients. Twenty children with mite allergy were studied. A hyperosmolar conjunctival challenge was performed before and after azelastine eye drops or placebo treatment for a period of 2 wk. It was found that patients treated with azelastine eye drops showed a significant reduction in nonspecific conjunctival hyperreactivity compared to the placebo group ($p = 0.018$). It was concluded that azelastine eye drops are able to reduce the nonspecific hyperreactivity present in subjects with mite allergy.
RE.CNT 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 17 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1998:500588 BIOSIS
DN PREV199800500588
TI Azelastine eye-drops in seasonal allergic conjunctivitis or rhinoconjunctivitis.
AU Giede-Tuch, C. [Reprint author]; Westhoff, M.; Zarth, A.
CS Lidenstr. 5, D-63450 Hanau, Germany
SO Allergy (Copenhagen), (Sept., 1998) Vol. 53, No. 9, pp. 857-862. print.
CODEN: LLRGDY. ISSN: 0105-4538.
DT Article
LA English
ED Entered STN: 18 Nov 1998
Last Updated on STN: 18 Nov 1998
AB This study was carried out to assess the efficacy of 0.025% and 0.05% azelastine eye-drops in patients with seasonal allergic conjunctivitis of gtoreq1 year's duration. A total of 151 patients received 0.025% or 0.05% azelastine eye-drops or placebo b.i.d. for 14 days according to a double-blind, randomized, placebo-controlled, parallel-dosing design; 129 patients completed the study as planned. The three target symptoms, scored on 4-point scales, were itching, lacrimation, and redness of the eyes; responders were patients whose symptom sum score decreased by gtoreq3 from a baseline score of gtoreq6 by day 3. Mean scores of these and five other symptoms were recorded also on days 7 and 14, and patients kept daily diaries of the three main symptoms and swollen eyelids. Responder rates were 73% for 0.025% (P=0.115 vs placebo) and 82% for 0.05% azelastine eye-drops (P=0.011 vs placebo) and 56% for placebo. The time courses of the mean (investigators' and patients') scores for the three main symptoms reflected the dose-dependent effect of azelastine eye-drops. One patient each from the two azelastine groups and three from the placebo group withdrew because of inefficacy. Adverse drug reactions were

reported by 14 and 24 patients receiving 0.025% and 0.05% azelastine eye-drops, respectively, and by eight placebo patients. These reactions were mainly slight application site reactions and taste perversion (bitter or unpleasant taste). Azelastine eyedrops are effective and well tolerated at a dose of 0.05% for the treatment of seasonal allergic conjunctivitis.

L4 ANSWER 18 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 10
AN 128:289947 CA
TI Dose-dependent protection by azelastine eye drops against pollen-induced allergic conjunctivitis. A double-blind, placebo-controlled study
AU Horak, Friedrich; Berger, Uwe Edwin; Menapace, Reinhard; Toth, Josef; Stuebner, Petra Ursula; Marks, Bernhardt
CS Ear Nose Throat Clinic, University Vienna, Vienna, A-1090, Austria
SO Arzneimittel-Forschung (1998), 48(4), 379-384
CODEN: ARZNAD; ISSN: 0004-4172
PB Editio Cantor Verlag
DT Journal
LA English
AB The efficacy and tolerability of azelastine (CAS 58581-89-8) eye drops at 3 different doses (0.025, 0.05, and 0.1%) were investigated in a double-blind, randomized, placebo-controlled, crossover study in 24 subjects with a history of allergic conjunctivitis/rhinoconjunctivitis, who were challenged, out of season, by airborne allergen in the "Vienna Challenge Chamber" (VCC). Subjects received a single dose of azelastine eye drops 60 min before the start of a 4 h challenge in the VCC. Addnl. local challenge, mimicking a gust of wind, was administered 15 min before the end of the session. Each of the 4 study days was separated by a 2 wk washout period. Azelastine eye drops showed a dose-dependent inhibition of the development of itching of the eyes. The effect was most pronounced 15 min after the addnl. local challenge. A maximal effect was achieved at a dose of 0.05%. Similar effects were observed on lacrimation. Azelastine eye drops also dose-dependently inhibited the degree of conjunctival redness, measured by digital imaging, and tended to reduce the low incidence of chemosis observed Ranking of the results of all symptoms for each treatment group confirmed the optimal effect at a dose of 0.05%. Azelastine eye drops had no effect on nasal and bronchial symptoms or on measurements of airways function (FEV1). No adverse effects of the treatments were reported. The data support the use of 0.05% azelastine eye drops in the treatment of allergic conjunctivitis/rhinoconjunctivitis.

L4 ANSWER 19 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 11
AN 130:75917 CA
TI Azelastine eye drops in the treatment of seasonal allergic conjunctivitis or rhinoconjunctivitis in young children
AU Sabbah, Alfred; Marzetto, Marcel
CS CHU d'Angers, Angers, F-49033, Fr.
SO Current Medical Research and Opinion (1998), 14(3), 161-170
CODEN: CMROCX; ISSN: 0300-7995
PB LibraPharm Ltd.
DT Journal
LA English
AB In a randomized, multicenter study, the effect of azelastine eye drops (n=51 patients) was compared in a double-blind manner with placebo eye drops (n = 30 patients) and in an open manner with levocabastine eye drops (n = 32 patients) during a 14-day treatment period involving 113 children (aged 4 to 12 yr) suffering from seasonal allergic conjunctivitis/rhinoconjunctivitis. The primary variable was the response rate defined as the number of patients showing an improvement after three days of treatment of at least three score points, from a min. baseline score of six, in the main ocular symptoms of itching, conjunctival redness and lacrimation (each assessed on a four-point scale). Patients discontinuing due to inefficacy were regarded as non-responders. The mean response rate in the azelastine eye drops group (74%) was significantly

higher (P<0.01) than that in the placebo group (39%) and comparable with that in the levocabastine group. The response rates assessed by the patients in their diaries were very similar. Significant differences (P < 0.01) for azelastine compared with placebo were observed on days 3 and 14 in the mean sum scores for the three main symptoms and for a total of eight eye symptoms. The overall assessment of efficacy confirmed the superiority of both active treatments compared with placebo. Adverse drug reactions were reported in 23% of placebo-, 35% of azelastine- and 38% of levocabastine-treated patients. These were mainly local irritant effects. Overall tolerability was assessed as very good or good in 80%, 84% and 91% of placebo-, azelastine- and levocabastine-treated patients, resp. Azelastine eye drops are effective and well-tolerated in children with seasonal allergic conjunctivitis.

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 12
AN 130:7369 CA
TI Physicochemical properties, NMR spectroscopy and tolerance of inclusion complexes of antazoline and tetracaine with hydroxypropyl-β-cyclodextrin
AU Van Santvliet, L.; Caljon, K.; Pieters, L.; Ludwig, A.
CS Department of Pharmaceutical Sciences, Laboratory of Pharmaceutical Technology and Biopharmacy, University of Antwerp (UIA), Antwerpen, B-2610, Belg.
SO International Journal of Pharmaceutics (1998), 171(2), 147-156
CODEN: IJPHDE; ISSN: 0378-5173
PB Elsevier Science B.V.
DT Journal
LA English
AB To improve the tolerance of **antazoline** and tetracaine **ophthalmic** solns., inclusion complexes of the free bases of both drugs with hydroxypropyl-β-cyclodextrin (HP-β-CD) were prepared The physicochem. properties of the drug:HP-β-CD solns. were determined and the inclusion complexes were characterized by 1H and 13C NMR spectroscopy. The apparent complex consts. were calculated from the phase-solubility diagram and were estimated at 403 M-1 and 1308 M-1 for the antazoline:HP-β-CD complex and tetracaine:HP-β-CD complex, resp. NMR anal. showed that in the 1:1 complexes the total antazoline fraction was present as an inclusion complex, whereas tetracaine was only partly included in spite of a similar phase solubility diagram. NMR spectroscopy also revealed the site of interaction of the drugs with the HP-β-CD mol. A solution acceptability test was carried out on volunteers. A relationship between the surface tension of the solns. and the tolerance was observed

RE.CNT 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1998:380424 BIOSIS
DN PREV199800380424
TI Azelastine eye drops reduce conjunctival non specific hyperreactivity in children with mite allergy.
AU Tosca, M. A.; Ciprandi, G.; Catrullo, A.; Cerqueti, P.; Mondino, C.; Passalacqua, G.; Canonica, G. W.
CS Allergy and Clinical Immunol. Serv., Dep. Internal Med., Genoa Univ., Genoa, Italy
SO Allergy (Copenhagen), (1998) Vol. 53, No. SUPPL. 43, pp. 116. print.
Meeting Info.: Annual Meeting of the European Academy of Allergology and Clinical Immunology. Birmingham, England, UK. June 21-26, 1998. European Academy of Allergology and Clinical Immunology.
CODEN: LLRGDY. ISSN: 0105-4538.
DT Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 2 Sep 1998
Last Updated on STN: 2 Sep 1998

L4 ANSWER 22 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1998:380280 BIOSIS
DN PREV199800380280
TI Investigation of the efficacy and tolerability of Azelastine, disodium cromoglycate and placebo eye drops in children with seasonal allergic conjunctivitis.
AU Khanferyan, R.; Sosnovikova, L.
CS Dep. Allergology Clinical Immunol., Kuban Med. Acad., Krasnodar, Russia
SO Allergy (Copenhagen), (1998) Vol. 53, No. SUPPL. 43, pp. 75. print.
Meeting Info.: Annual Meeting of the European Academy of Allergology and Clinical Immunology. Birmingham, England, UK. June 21-26, 1998. European Academy of Allergology and Clinical Immunology.
CODEN: LLRGDY. ISSN: 0105-4538.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 2 Sep 1998
Last Updated on STN: 2 Sep 1998

L4 ANSWER 23 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 13
AN 126:242892 CA
TI Ophthalmic pharmaceuticals containing O-carboxyalkyl chitosan
IN Reed, Kenneth W.; Yen, Shau-Fong
PA Ciba-Geigy A.-G., Switz.; Reed, Kenneth W.; Yen, Shau-Fong
SO PCT Int. Appl., 25 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9706782	A1	19970227	WO 1996-EP3477	19960806
	W: AL, AU, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	TW 389694	B	20000511	TW 1995-84113923	19951227
	AU 9667897	A1	19970312	AU 1996-67897	19960806
	EP 844868	A1	19980603	EP 1996-928418	19960806
	EP 844868	B1	20011024		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11510497	T2	19990914	JP 1997-507926	19960806
	AT 207343	E	20011115	AT 1996-928418	19960806
	PT 844868	T	20020328	PT 1996-928418	19960806
	ES 2166905	T3	20020501	ES 1996-928418	19960806
PRAI	US 1995-516420	A	19950817		
	WO 1996-EP3477	W	19960806		

AB Ophthalmic pharmaceuticals containing O-carboxyalkyl chitosan (I) are disclosed. I enhances ocular bioavailability and is especially useful in ophthalmic compns. which must be held at an acidic pH for storage, and which must remain clear when applied to the eye at a physiol. pH of about 7.4. An ophthalmic solution contained glacial acetic acid 5, sodium chloride 6, N,O-carboxymethyl chitosan 40, pilocarpine 20 g, and water 900 mL; pH = 5. The composition performed similarly to Sperasacarpine (containing 4.5 mg/mL

HPMC) in miosis profile as a function of time.

L4 ANSWER 24 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 14
AN 126:162281 CA
TI Ophthalmic compositions and methods for stabilizing polymers
IN Tsao, Fu-Pao
PA Ciba-Geigy A.-G., Switz.; Tsao, Fu-Pao
SO PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9700669	A1	19970109	WO 1996-EP2539	19960612
	W: AL, AU, BB, BG, BR, CA, CN, CZ, EE, GE, HU, IL, IS, JP, KP, KR, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	US 5683993	A	19971104	US 1995-493761	19950622
	CA 2222646	AA	19970109	CA 1996-2222646	19960612
	AU 9663551	A1	19970122	AU 1996-63551	19960612
	AU 715686	B2	20000210		
	EP 833609	A1	19980408	EP 1996-922797	19960612
	EP 833609	B1	20011107		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 11510480	T2	19990914	JP 1997-503430	19960612
	AT 208189	E	20011115	AT 1996-922797	19960612
	PT 833609	T	20020429	PT 1996-922797	19960612
	ES 2167581	T3	20020516	ES 1996-922797	19960612
	US 5858996	A	19990112	US 1997-863855	19970527
PRAI	US 1995-493761	A2	19950622		
	WO 1996-EP2539	W	19960612		

AB Ophthalmic compns. and methods for reducing the decomposition rate of polymeric bioadhesives and viscosity enhancers, such as poly(acrylic acids) are described. The compns. include at least 1 strong, stable chelating agent, preferably an organophosphorous compound such as diethylenetriamine pentamethylene phosphonic acid. Thus, a composition was prepared by mixing Noveon AA1 0.625, NaCl 0.6, PEG 400 0.2, Dequest 2060 0.006, and Dextran 70 0.1%, and qs water. The pH of the solution was adjusted to 6.8, and the viscosity of the composition was determined

L4 ANSWER 25 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 15
AN 128:80036 CA
TI Ophthalmic pharmaceutical composition
IN Kang, Meng-Che
PA Taiwan
SO U.S., 3 pp.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 5698533	A	19971216	US 1994-280827	19940726
	GB 2302018	A1	19970108	GB 1995-11983	19950613
	GB 2302018	B2	19990825		
	DE 19521684	A1	19961219	DE 1995-19521684	19950614
	DE 19521684	C2	19990902		
	JP 09002944	A2	19970107	JP 1995-186115	19950620
	JP 2797069	B2	19980917		

PRAI US 1994-280827 19940726
AB A method of administering a drug to an eye consists of admixing a hydrocarbon semi-solid or oil which contains the drug with water at a temperature above the m.p. of the semi-solid or oil, nebulizing the admixt. to form liquid drops and applying the liquid drops to the eye. Thus, a formulation for treating the dry eye syndrome contained petrolatum 94, camphor 5, and menthol 1 g, and vitamin A 500,000 IU.

L4 ANSWER 26 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 16
AN 126:255503 CA
TI Ophthalmic compositions containing hydrocarbonaceous carrier
IN Kang, Meng-Che
PA Kang, Meng-Che, Taiwan
SO Brit. UK Pat. Appl., 12 pp.
CODEN: BAXXDU
DT Patent
LA English
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	GB 2302018	A1	19970108	GB 1995-11983	19950613
	GB 2302018	B2	19990825		
	US 5698533	A	19971216	US 1994-280827	19940726

PRAI US 1994-280827 19940726
AB Compns. contain 0.01-20% drug and 80-99.99% of a hydrocarbonaceous carrier which is a semisolid at room temperature and melts at 30-100°. Typical carriers are petrolatum or lanolin. An emulsifier is optionally present. Suitable drugs for inclusion in the compns. are also listed. Delivery to the eye is particularly in nebulized form. Compns. containing vitamin A and vitamin B12 as active ingredients are exemplified. An ophthalmic composition contained petrolatum 94, camphor 5, menthol 1 g, vitamin A 500,000 IU.

L4 ANSWER 27 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 17
AN 126:108926 CA
TI Semisolid hydrocarbon carrier for ophthalmic spray
IN Kang, Meng-Che
PA Kang, Meng-Che, Taiwan
SO Ger. Offen., 4 pp.
CODEN: GWXXBX
DT Patent
LA German
FAN.CNT 3

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 19521684	A1	19961219	DE 1995-19521684	19950614
	DE 19521684	C2	19990902		
	US 5698533	A	19971216	US 1994-280827	19940726

PRAI US 1994-280827 19940726
AB A semisolid hydrocarbon carrier containing an ophthalmic drug is mixed with water at a temperature above the m.p. of the carrier and atomized (e.g. by sonication) to form liquid droplets which are directed to the eye without use of chlorofluorocarbon propellants. The drug may be especially an agent for relief of dry eye syndrome, an astringent, an antimicrobial agent, etc. Thus, a composition for treatment of dry eye syndrome, containing petrolatum 94,
camphor 5, menthol 1 g, and vitamin A 500,000 IU, was melted in 5 g water at 60° and atomized to form droplets with a hydrophilic core and a lipophilic shell.

L4 ANSWER 28 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 18
AN 122:197117 CA
TI Synthesis and Identification of the Primary Degradation Product in a Commercial Ophthalmic Formulation Using NMR, MS, and a Stability-Indicating HPLC Method for Antazoline and Naphazoline

AU Ruckmick, Stephen C.; Marsh, Dennis F.; Duong, San T.
CS Allergan Pharmaceuticals, Irvine, CA, 92713-9534, USA
SO Journal of Pharmaceutical Sciences (1995), 84(4), 502-7
CODEN: JPMSAE; ISSN: 0022-3549
PB American Chemical Society
DT Journal
LA English
AB HPLC anal. of an anti-infective ophthalmic solution (Albalon-A), containing the active drugs naphazoline and antazoline, revealed a degradation peak of unknown identity. To elucidate the identity of the degradant, the active drugs were each hydrolyzed by refluxing at high pH, and their resp. hydrolysis products were isolated and spectrally characterized by NMR, FT-IR, and MS for conclusive structure elucidation. The degradant's identity was confirmed by HPLC-MS anal. of Albalon-A **ophthalmic** solution to be the **antazoline** hydrolysis product N-[(N-benzylanilino)acetyl]ethylenediamine (I). A stability-indicating HPLC method was then developed which was able to resolve I from the active drugs. This HPLC method was then validated for quantitating the active drugs and I. Validation studies demonstrated linear UV response at 280 nm, recovery > 98%, good reproducibility, and a detection limit of 2 μg/mL I. Overall, the data demonstrated that the HPLC method was quant. and specific for antazoline, naphazoline, and I. Anal. of an expired stability lot of the ophthalmic solution indicated the concentration of I was 0.002% (weight/volume).

L4 ANSWER 29 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 19
AN 124:332217 CA
TI Aesthesiometry-azelastine eye drops reduce corneal sensitivity in rabbits, but not in dogs and humans
AU Krauser, Klaus; Schneider, Edith; Hermann, Robert; Jahn, Wolfgang
CS Institute Toxicology, ASTA Medica AG, Halle/Saale, D-33790, Germany
SO Ocular Toxicology, [Proceedings of the Congress of International Society of Ocular Toxicology], 4th, Annecy, Fr., Oct. 9-13, 1994 (1995), Meeting Date 1994, 287-295. Editor(s): Weisse, Ingo. Publisher: Plenum, New York, N. Y.
CODEN: 62SPAL
DT Conference
LA English
AB **Azelastine ophthalmic** solns., which have good antiallergic efficacy, have hypoesthetic activity in the cornea of rabbit eyes but not in the eyes of dogs or humans. Thus, in the rabbit, the susceptibility of the cornea to substances with a hypoesthetic activity is obviously much higher than in other species, and so the rabbit should not to predict results in man.

L4 ANSWER 30 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 20
AN 122:89492 CA
TI **Azelastine ophthalmic** compositions
IN Sanuki, Daizaburo; Orihashi, Masahiro
PA Teika Seiyaku Kk, Japan
SO Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	JP 06298649	A2	19941025	JP 1993-116510	19930419
PRAI	JP 1993-116510		19930419		

AB **Ophthalmic** compns. contain **azelastine** HCl (I), as an allergy inhibitor, and boric acid, glutamic acid, or their salts. An ophthalmic composition containing I 25, boric acid 1500, Na glutamate 200, mannitol

100, chlorobutanol 100 mg, aqueous 0.001 N HCl, 0.1% benzalkonium chloride solution, and H2O to 100 mL was nonirritant to the mucous membrane of rabbit eyes. Administration of the composition (at 25 μL once a min for 10 times) to rats inhibited egg white albumin-induced allergy by 57.4%.

L4 ANSWER 31 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 21
AN 120:144186 CA
TI Stable preparation containing azelastine hydrochloride
IN Morita, Yutaka; Koyama, Noritosi; Ohsawa, Sigemitu
PA ASTA Medica AG, Germany; Eisai Co., Ltd.
SO Eur. Pat. Appl., 12 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 580074	A1	19940126	EP 1993-111334	19930715
	EP 580074	B1	19950118		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
	JP 06040949	A2	19940215	JP 1992-213243	19920720
	JP 3190441	B2	20010723		
	ES 2068725	T3	19950416	ES 1993-111334	19930715
	US 6117864	A	20000912	US 1997-889807	19970708
PRAI	JP 1992-213243	A	19920720		
	US 1993-92998	B1	19930719		
	US 1995-376659	B1	19950120		

AB A stable preparation which does not produce crystalline hydrates and has excellent
percutaneous and mucosal absorbability, comprises azelastine·HCl (I) and a ≥8 C fatty acid and is adjusted to pH 6-9. The preparation further contains ≥1 ingredients selected from the group consisting of ethanol, isopropanol, polyhydric alcs., and lecithins. For example, a lotion containing I 0.3 g, myristic acid 0.28 g, ethanol 10 mL, purified water to 100 mL, and NaOH q.s. to pH 7.5 was formulated and packaged in glass containers. After storage in a refrigerator, at room temperature, or in an incubator at 45° for 2 mo, no azelastine hydrates were observed

L4 ANSWER 32 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 22
AN 117:239953 CA
TI Liquid chromatographic assay for naphazoline and **antazoline** in **ophthalmic** preparations
AU Bocic, Ronny; Vallejos, Cristobal; Alvarez-Lueje, Alejandro; Lopez, Fernando
CS Fac. Cienc. Quim. Farma. Farmacoquim. Anal. Med., Univ. Chile, Santiago, Chile
SO Journal of AOAC International (1992), 75(5), 902-4
CODEN: JAINEE; ISSN: 1060-3271
DT Journal
LA English
AB A liquid chromatog. (LC) anal. was developed for determining naphazoline and **antazoline** in **ophthalmic** prepns. The LC system was designed so that a variety of **ophthalmic** solns. containing naphazoline and **antazoline** can be analyzed with precision.

L4 ANSWER 33 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1990:289615 BIOSIS
DN PREV199090020461; BA90:20461
TI EFFECTS OF VASOCON A IN THE ALLERGEN CHALLENGE MODEL OF ACUTE ALLERGIC CONJUNCTIVITIS.
AU ABELSON M B [Reprint author]; PARADIS A; GEORGE M A; SMITH L M; MAGUIRE L; BURNS R
CS 20 STANIFORD ST, BOSTON, MASS 02114, USA

SO Archives of Ophthalmology, (1990) Vol. 108, No. 4, pp. 520-524.
CODEN: AROPAW. ISSN: 0003-9950.
DT Article
FS BA
LA ENGLISH
ED Entered STN: 23 Jun 1990
Last Updated on STN: 7 Aug 1990
AB The ophthalmic combination product of 0.05% naphrazoline hydrochloride and 0.5% antazoline phosphate (Vasocon-A) was evaluated as an antiallergic agent in 100 subjects with a known allergic history to cat dander, ragweed, or bluegrass pollen. Three independent study sites were used. The allergen challenge model of acute allergic conjunctivitis was selected to assess the agent as it provided a standardized and precise way to measure drug effectiveness for this indication. In a double-masked randomized fashion, the subjects were assigned to one of three groups that received one drop of Vasocon-A in one eye and one drop of either 0.05% naphazoline (group 1), 0.5% antazoline (group 2), or placebo (group 3) in the contralateral eye. After 10 minutes, the dose of allergen shown to elicit a 2+ redness and itching reaction was instilled bilaterally. Signs and symptoms of allergic conjunctivitis were evaluated after 3, 5, and 10 minutes. Subjects were then rechallenged 2 hours after drug administration to assess the duration of action of the agents. Vasocon-A was found to significantly inhibit all five major signs and symptoms of allergic conjuctivitis: itching, redness, chemosis, lid swelling, and tearing, for more than 85% of the comparisons when compared over time with placebo, naphazoline alone, or antazoline alone. The results of this study indicate that the combination of naphazoline and antazoline was more effective in inhibiting redness than naphazoline and more effective in inhibiting itching than antazoline. These findings support the use of such a combination for the treatment of allergic conjunctivitis.

L4 ANSWER 34 OF 42 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
AN 1990-23043 DRUGU A G
TI Use of Partition Chromatography in the Analysis of Naphazoline-Antazoline and Pseudoephedrine-Carbinoxamine in Pharmaceutical Products. (Sp.).
AU Lopez Silva F; Bocic Vildosola R; Vallejos Ramos C; Alvarez Lueje A
LO Santiago, Chile
SO An.R.Acad.Farm. (56, No. 1, 19-27, 1990) 6 Tab. 17 Ref.
CODEN: ARAFAY ISSN: 0034-0618
AV No Reprint Address
LA Russian
DT Journal
FA AB; LA; CT; MPC
FS Literature
AB A method for the separation and quantitative determination of mixtures of naphazoline HCl with antazoline phosphate and of pseudoephedrine HCl with carbinoxamine maleate, is described. The components of the mixtures were separated by liquid chromatography on a Kieselguhr column support with a stationary phase of phosphate buffer (pH 6.0) and mobile phase of chloroform. The resolved drugs were determined by UV spectrophotometry at the respective absorbance wavelengths. The method was applied to determination of naphazoline and **antazoline** in **ophthalmic** solutions and pseudoephedrine and carbinoxamine in oral drops solution as a respiratory decongestant with good accuracy and precision.

L4 ANSWER 35 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 23
AN 112:84186 CA
TI Nasal and eye preparations containing azelastine salts
IN Hettche, Helmut
PA Asta Pharma A.-G., Fed. Rep. Ger.
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent

LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	DE 3836579	A1	19890524	DE 1988-3836579	19881027
	EP 316633	A1	19890524	EP 1988-117902	19881027
	EP 316633	B1	19930127		
	R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	AT 84968	E	19930215	AT 1988-117902	19881027
	ES 2053678	T3	19940801	ES 1988-117902	19881027
	JP 01153639	A2	19890615	JP 1988-282639	19881110
	JP 2911460	B2	19990623		
	CA 1319322	A1	19930622	CA 1988-582817	19881110
	DK 8806301	A	19890514	DK 1988-6301	19881111
	DK 174928	B1	20040301		
	AU 8825063	A1	19890518	AU 1988-25063	19881111
	AU 613107	B2	19910725		
	ZA 8808461	A	19890830	ZA 1988-8461	19881111
	US 5164194	A	19921117	US 1990-551644	19900712
	JP 10182464	A2	19980707	JP 1997-359963	19971226
	JP 2956029	B2	19991004		
	JP 11349484	A2	19991221	JP 1999-19955	19990128
	JP 3207816	B2	20010910		
PRAI	DE 1987-3738681	A1	19871113		
	EP 1988-117902	A	19881027		
	US 1988-268772	B1	19881109		
	JP 1988-282639	A3	19881110		

AB Azelastine (I) salts are formulated as nasal or eye prepns. Use of these prepns. avoids the bitter taste associated with oral I administration, such as in the treatment of asthma and allergy. A nasal spray (pH 6.8) comprised I-HCl 10, di-Na edetate 5, NaCl 68, benzalkonium chloride 1.25, citric acid 4.38, Na2HPO4 64.8, and Methocel E4M 10 g, in 10 L aqueous solution

L4 ANSWER 36 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 24
AN 107:121207 CA
TI Direct determination of antazoline and naphazoline in mixtures
AU Othman, S. O.
CS Res. Dev. Dep., Dar Al-Dawa Dev. Investment Co., Na'ur, Jordan
SO Drug Development and Industrial Pharmacy (1987), 13(7), 1257-65
CODEN: DDIPD8; ISSN: 0363-9045
DT Journal
LA English
AB The simultaneous determination of **antazoline** and naphazoline in nasal and **ophthalmic** mixts. was achieved using a direct and simple spectrophotometric method. The absorbance of a suitable dilution of the mixture was measured at two wavelengths, 271 and 281 nm, and the concentration of
each in the mixture was calculated by solving two simultaneous equations. The choice of wavelengths was such that antazoline shows weak absorption while naphazoline exhibits maximal absorption. The method proved to be simple and rapid with a good degree of reproducibility.

L4 ANSWER 37 OF 42 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
AN 1987-37453 DRUGU T S E
TI A Comparison of Budesonide and Beclomethasone Dipropionate Nasal Aerosols in Ragweed-Induced Rhinitis.
AU Vanzieleghem M A; Juniper E F
LO Hamilton, Ontario, Canada
SO J.Allergy Clin.Immunol. (79, No. 6, 887-92, 1987) 4 Fig. 2 Tab. 20 Ref.
CODEN: JACIBY ISSN: 0090-7421
AV Firestone Regional Chest and Allergy Clinic, St. Joseph's Hospital, 50 Charlton Ave. East, Hamilton, Ontario, Canada L8N 4A6.
LA English
DT Journal

FA AB; LA; CT
FS Literature
AB In a double-blind, random study in 61 patients treated for seasonal allergic rhinitis due to a ragweed-pollen, budesonide (BU) aerosol inhalation demonstrated better clinical potency than beclomethasone (BE). Side effects included stinging of the nasal mucosa on application, headache and with BU nasal bleeding. Chlorpheniramine maleate (CH) was given if treatment was inadequate. Eye symptoms were controlled with a naphazoline HCl-**antazoline ophthalmic** drop preparation and medrysone eye drops. Salbutamol (SA) was given for asthma.

L4 ANSWER 38 OF 42 CA COPYRIGHT 2004 ACS on STN DUPLICATE 25
AN 106:23348 CA
TI Simultaneous high-performance liquid chromatographic determination of **antazoline** phosphate and tetrahydrozoline hydrochloride in **ophthalmic** solution
AU Puglisi, Giovanni; Sciuto, Sebastiano; Chillemi, Rosa; Mangiafico, Sebastiano
CS Ist. Chim. Farm. Tossicol., Univ. Catania, Catania, Italy
SO Journal of Chromatography (1986), 369(1), 165-70
CODEN: JOCRAM; ISSN: 0021-9673
DT Journal
LA English
AB A reversed-phase ion-pair HPLC method was used for simultaneous determination of
antazoline (I) [91-75-8] (as phosphate) and tetrahydrozoline (II) [84-22-0] (as HCl salt) in ophthalmic solns. A Hypersil C8 column was used and the solvent system consisted of MeCN-MeOH (1:1) and 0.005M octanesulfonic acid Na salt in aqueous 0.005M di-Na phosphate (pH 7). The absorbance was measured at 222 nm. Dimethylaminobenzaldehyde was used as the internal standard The method was simple, rapid, sensitive and precise with relative standard deviations of 0.45-0.62%.

L4 ANSWER 39 OF 42 DRUGU COPYRIGHT 2004 THE THOMSON CORP on STN
AN 1984-21481 DRUGU T M
TI Corneal Disease: An Approach to Primary Care.
AU Schlichtemeier W R
LO Omaha, Nebraska, United States
SO Geriatrics (39, No. 1, 58-61, 64-66, 1984) 7 Fig. 9 Ref.
CODEN: GERIAZ ISSN: 0016-867X
AV Ophalmology, 818 Doctors Building, 4239 Farnam Street, Omaha, NE 68131, U.S.A.
LA English
DT Journal
FA AB; LA; CT
FS Literature
AB Approaches to primary care of corneal disease were reviewed. Treatment of ocular fungal, herpetic or bacterial infection, trauma, hereditary and degenerative corneal dystrophies were considered.

L4 ANSWER 40 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1981:156680 BIOSIS
DN PREV198171026672; BA71:26672
TI EFFECTS OF TOPICALLY APPLIED OCULAR DECONGESTANT AND ANTIHISTAMINE.
AU ABELSON M B [Reprint author]; ALLANSMITH M R; FRIEDLAENDER M H
CS EYE RES INST, 20 STANIFORD ST, BOSTON, MASS 02114, USA
SO American Journal of Ophthalmology, (1980) Vol. 90, No. 2, pp. 254-257.
CODEN: AJOPAA. ISSN: 0002-9394.
DT Article
FS BA
LA ENGLISH
AB In 2 independent studies including 25 subjects each, naphazoline caused

significant whitening (but did not prevent itching) in the histamine-induced red, itchy eye. Antazoline inhibited itching (but not redness) to a significant degree in the same model. The combination of naphazoline and antazoline produced significant whitening and inhibition of itching in all eyes challenged by histamine. The combination of the 2 drugs was more effective than either component alone in preventing redness. The antihistamine and combination of antihistamine/vasoconstrictor were equally effective in arresting itching.

L4 ANSWER 41 OF 42 USPATFULL on STN
AN 78:33582 USPATFULL
TI Method of lowering intraocular pressure with antazoline
IN Salem, Harry, Elkins Park, PA, United States
Aviado, Domingo M., Wynnewood, PA, United States
PA Cooper Laboratories, Incorporated, Parsippany, NJ, United States (U.S. corporation)
PI US 4097577 19780627
AI US 1976-713805 19760812 (5)
DT Utility
FS Granted
EXNAM Primary Examiner: Friedman, Stanley J.; Assistant Examiner: Robinson, D. W.
LREP Boland, Thomas R., Kolano, John J.
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 225
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for lowering intraocular pressure in mammals by administering thereto an effective amount of antazoline, i.e., 2-(N-benzylanilinomethyl)-2-imidazoline or its pharmacologically acceptable acid addition salts, preferably antazoline phosphate.

L4 ANSWER 42 OF 42 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
AN 1983:242701 BIOSIS
DN PREV198376000193; BA76:193
TI TREATMENT OF ALLERGIC CONJUNCTIVITIS WITH OCULAR DECONGESTANTS.
AU SMITH J P [Reprint author]; LANIER B Q; TREMBLAY N; WARD R L; DEFALLER J M
CS NEW PRODUCT RES-MED DEP, ALCON LABS INC, 6201 S FREEWAY, PO BOX 1959, FORT WORTH, TEX 76101, USA
SO Current Eye Research, Vol. 2, No. 2, pp. 141-147. 1982-1983.
CODEN: CEYRDM. ISSN: 0271-3683.
DT Article
FS BA
LA ENGLISH
AB Three commercially available ocular decongestant products which contain varying concentrations of a vasoconstrictor (naphazoline hydrochloride) and an antihistamine (antazoline phosphate or pheniramine maleate) were tested for comfort and therapeutic efficacy. Three separate studies were performed: a comfort comparison, a vasoconstrictive efficacy test using an in vivo model of allergic conjunctivitis induced by compound 48/80 [product of 4-', methoxy-N-methylbenzene methyl-anamine and formaldehyde], and a clinical trial of therapeutic efficacy in patients with allergic/hay fever conjunctivitis. The 3 preparations varied greatly in patient comfort and acceptability but were not different in their ability to ameliorate the itching, tearing, redness, edema and discomfort that occur in human allergic conjunctivitis.